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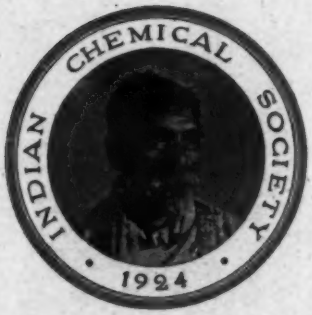

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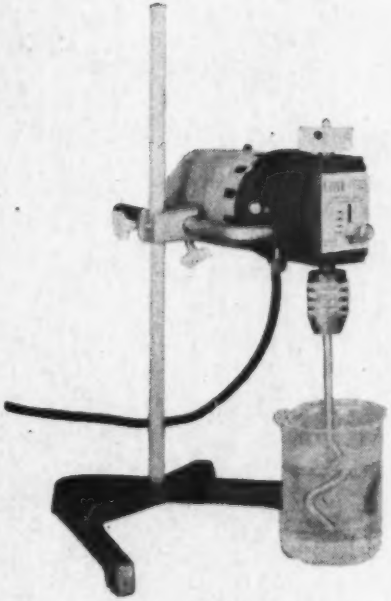

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JOURNAL OF THE INDIAN CHEMICAL SOCIETY

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FOR AUTHORS ONLY

*Extracts from the "Style Guide for Chemists" by Fieser & Fieser will be published henceforth in each issue of this Journal so that authors may take advantage in improving the quality of their composition and presentation.

3.2. Intransitive verbs (cannot have an object and cannot have a passive voice).

autoxidize	flow
effervesce	react
fall	rise

The only verb in this list that causes trouble is *react*. Grammarians regard the verb as intransitive and frown on "Baeyer reacted phenol with aldehydes" ("Baeyer studied the reaction of phenol with aldehydes") and "The alkaloid *was reacted* with one equivalent of....." ("*was allowed to react*.....", "*was caused to react with*.....", or "*was treated with*"). Agreed. And if *react* is intransitive, it has no passive voice and the word *unreacted* is incorrect: ".....recovered only unreacted hydrocabon." Fortunately, technically correct substitutes are available: *unchanged, unaltered.*

3.3. Verb that are either transitive or intransitive.

coagulate	dimerize, polymerize	isomerize
condense	distil	precipitate
cool, heat	drop	rearrange
crystallize	filter	reflux
decompose	ionize	separate

Some verbs that were originally intransitive have acquired a more or less metaphorical transitive meaning, and some transitive verbs have become intransitive as well. Dictionaries are not infallible guides to correct verb form: they often indicate what is used and not what should be used. According to Webster, *acetylate* is transitive or intransitive, but the related word *acylate* is transitive only.

3.4. The active voice is usually more direct and vigorous than the passive (Strunk).

The passive voice is unavoidable in chemical writings because the majority of the verbs describing reactions and operations are transitive: the active voice necessitates use of "I" or "the operator". We prefer to say "Benzene is sulfonated readily" rather than "One can sulfonate benzene readily". However, the active voice, where possible, is to be preferred: it is stronger than the passive, and it is likely to be free from incoherent, dangling, and lengthy expressions often associated with the passive voice.

Passive	Active
It will be seen from the tables.....	The tables show.....
The rearrangement has been shown by X to take place with inversion.	X established that the rearrangement takes place with inversion.
There were a number of fractions which remained noncrystalline.	A number of fractions failed to crystallize.
At the beginning of the distillation droplets of water could be observed to form.	Droplets of water appeared at the beginning of the distillation.
Our reason for suspecting the presence of a diene was that a deep coloration in the tetranitromethane test was noted.	A deep coloration in the tetranitromethane test suggested the presence of a diene.
Chaulmoogric acid was named from the name of an East Indian tree.	Chaulmoogric acid takes its name from that of an East Indian tree.

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[Jour. Indian Chem. Soc., Vol. 38, No. 4, 1961]

Constitutional Problems Concerning Anthraquinonoid Vat Dyes*

K. Venkataraman

At meetings of the Dyestuffs Exploratory Committee set up by the Govt. of India in 1941 and during discussions between an Indian and a British firm at about the same time, I put forward the somewhat heterodox view that anthraquinonoid vat dyes and azoic components, rather than the direct cotton dyes and Sulphur Black, should be produced in the first phase of a 10 or 15-year plan for a dyestuff industry in India. The proposition was justified by the fact that the cotton textile industry, the largest of all Indian industries, increasingly demanded shades of all-round fastness, which could only be obtained from the anthraquinonoid vat dyes and the azoic dyes. Apart from their technical importance, the anthraquinonoid vat dyes are of interest to the organic chemist because they include many complex homocyclic and heterocyclic compounds and offer numerous problems for investigation from the point of view of structure determination, degradation methods, synthetical reactions, and relationships between chemical constitution and colour, affinity for cellulose, and fastness properties. Simultaneously with attempts to stimulate interest in the production of vat dyes in India, work on a few problems in this vast area was undertaken by a small group in the University of Bombay.

Chromatographic Analysis

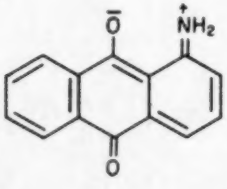
Vat dyes are insoluble in water and water-soluble impurities can therefore be readily removed. The nonvattable impurities are also easy to remove by reduction with sodium hydrosulphite in aqueous sodium hydroxide, filtration, and reoxidation by air; but the possibility of permanent chemical changes, such as dehalogenation, reduction of nitro groups, and hydrolysis of amide groups should be borne in mind. The isolation of the main constituent of a commercial vat dye may involve separation from other vat dyes added for shading purposes. Because of the sparing solubility of the anthraquinonoid vat dyes in organic solvents, chromatographic separation has to be carried out at high temperatures, using high-boiling solvents such as *o*-dichlorobenzene, 1,2,4-trichlorobenzene, molten naphthalene, phenol, and cresols. A simple apparatus and procedure for this purpose were described in a recent paper[1]. Solutions of the leuco derivatives of vat dyes in aqueous sodium hydroxide are unsuitable for paper chromatography because of their rapid oxidation to the insoluble quinones; but when sodium hydroxide is replaced by aqueous tetraethylenepentamine, $NH_2(CH_2CH_2NH)_3CH_2CH_2NH_2$, reduction with sodium hydrosulphite yields a clear and very stable vat. The solution can be submitted to paper chromatography or chromatographed on a column of cellulose powder, the same reagents in aqueous solution being employed for developing the chromatogram[2].

Absorption Spectra of Leuco Derivatives

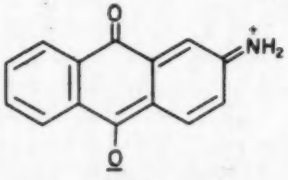
In connection with the constitution of lac dye constituents it was observed that the spectra of the leuco derivatives in alkaline solution are useful for distinguishing between hydroxynaphthaquinones and hydroxyanthraquinones; the former have an absorption maximum at about 390 mμ; the latter exhibit a maximum in the 420-450 mμ region, together in some cases with a broad diffuse band in the 500 mμ region[3]. The absorption spectra of the leuco derivatives of anthraquinonoid vat dyes in sodium hydroxide solution are of limited value for their characterization. Waters[4] has stated that in pursuance of a general programme of research on the dyeing of cellulose he carried

* Presidential address delivered at the 37th Annual General Meeting of the Indian Chemical Society, held at Roorkee on Thursday, January 5, 1961.

out measurements of the absorption spectra of various vat dyes in both the reduced and oxidised states; but the only dye for which the absorption curves were given was Caledon Yellow 3G (1,5-bisbenzamidoanthraquinone). Waters observed a characteristic similarity in the absorption spectra of the reduced dyes, referring presumably to the benzamidoanthraquinones he examined; there were two distinct absorption bands with maxima in the blue and yellow regions. One difficulty in the determination of the spectra of the leuco derivatives in alkaline solution is their oxidisability, but this is overcome by the addition of ethanol or dioxane. The spectra of the sodium salts of the leuco derivatives of anthraquinone, 1- and 2-aminoanthraquinone, and a series of acylamidoanthraquinones were determined by Padhye *et al.*, who found that the spectrum of anthrahydroquinone did not undergo any characteristic change by the substitution of an amino or a benzamido group in the 1- or 2-position[5]. The spectrum of anthraquinone in the reduced state shows one sharp peak of high intensity at 420 mμ (A band) and a broad diffuse band at about 506 mμ (B band). On the introduction of an amino group in the 1- or 2-position, no major change in the nature of the spectra of the reduced compounds is observed. The oxidised compounds behave very differently, profound changes in the absorption spectra occurring when anthraquinone is substituted by an amino group in the 1- or 2-position. This is understandable if we associate the colour of the aminoanthraquinones with the contribution of low-energy structures, such as (I) and (II), to the excited states of the molecules[6]. In the alkaline solutions of the leuco derivatives of anthraquinone and the aminoanthraquinones, the absorption spectra are those of the anions of anthrahydroquinones. The negatively charged oxygen atoms inhibit the contribution of structures involving positively charged nitrogen, and as a result there is little or no electronic interaction between the amino group and the anthrahydroquinone nucleus as in structures (I) and (II). The amino group will then show presumably an effect like the anilinium ion or the amino group in 2,6-dimethylaniline, because of restricted electron mobility. The A band of leuco anthraquinone is shifted to 430 mμ in leuco 1-aminoanthraquinone; in leuco 2-aminoanthraquinone there is a hypsochromic shift to 418 mμ. The B band of the leuco anthraquinone spectrum at 506 mμ undergoes reverse changes, the 1-amino compound showing a hypsochromic shift and the 2-amino compound a bathochromic shift.



(I)



(II)

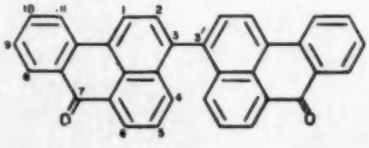
The introduction of one or more benzamido groups in the α- or β-position does not effect any change in the nature of the spectrum, except for shifts in the wave lengths of maximum absorption. The spectrum of leuco 1-benzamidoanthraquinone shows that the A band is at about 425 mμ as in the spectrum of leuco 1-aminoanthraquinone, and has the same order of intensity. The B band, which does not show an appreciable shift in the 1-amino compound as compared with anthraquinone, has shifted considerably to the longer wave length side and has a slightly greater intensity than the corresponding band for leuco 1-aminoanthraquinone. The A band of leuco anthraquinone shows a much greater bathochromic shift in the 2-benzamido than in the 1-benzamido derivative, but there is little increase in intensity. There is no distinct B band in the spectrum of leuco 2-benzamidoanthraquinone corresponding to the B band of leuco anthraquinone, although there is a flat absorption in this region which shows the presence of

this band. In leuco 2-benzamidoanthraquinone the A band, which does not show any shift in leuco 2-aminoanthraquinone as compared with leuco anthraquinone, exhibits a considerable shift and has about the same order of intensity. Thus it is principally one of the two bands (A or B) of leuco anthraqinone, which shifts on substitution of an amino group in the 1- or 2-position; on benzoylation the position of this displaced band remains nearly the same, but the second band undergoes a bathochromic shift. Further introduction of a benzamido group in the 4- or 5-position of 1-benzamidoanthraquinone decreases the intensity of absorption, this decrease being considerable in the case of leuco 1,5-bisbenzamidoanthraquinone; the wave lengths of the absorption maxima are also shifted, although not very significantly.

Steric Hindrance in Dibenzanthronyls and Dibenzanthrones

There are many examples of the effect of steric hindrance to planarity on the absorption spectra of organic molecules. A common effect of such steric hindrance is a reduction in the intensity of maximum absorption, usually, but not invariably, accompanied by a hypsochromic shift in the long wave length absorption. Changes in the absorption spectra as a result of steric hindrance to planarity can be related to its interference with the resonance of the molecule either in the ground state or excited state. Steric hindrance in the excited state decreases the resonance stabilization of that state and increases the transition energy, leading therefore to a hypsochromic shift in the absorption spectrum. On the other hand, steric hindrance in the ground state decreases the energy of transition because of the reduced resonance stabilization of the ground state, and the consequence is a bathochromic shift in the absorption spectrum. In a review of the effects of steric hindrance to planarity of dye molecules, Brooker[7] has discussed two distinct types of behaviour. Most of the compounds studied were characterized by a single low-energy resonance structure. As a rule the crowding substituent does not affect this single dominant structure, which is usually benzenoid contributing principally to the ground state, but affects other high-energy structures, which contribute mostly to the excited states of the molecule, resulting in a hypsochromic shift of the spectrum. But where the molecule can be represented by two identical structures of low energy, the effect of steric hindrance is to decrease the contribution of these identical structures to the ground state of the molecule, thereby leading to a bathochromic shift.

The effect of steric factors on the absorption spectra of diphenyl derivatives has been thoroughly investigated[8]. When the two benzene rings are forced into different planes as in dimesityl, the absorption corresponds to that of mesitylene ($\epsilon \times 2$). Friedel *et al.* have discussed the effects of steric hindrance on the spectra of the three dinaphthyls and they have shown that the effect of steric hindrance in 1,1′-dinaphthyl results in a spectrum very similar to that of naphthalene, except for the relative absence of fine structure. The spectra of benzanthrone, 3,3′-dibenzanthronyl (III), and 4,4′-dibenzanthronyl (IV) are very similar, indicating that in the two latter compounds there is no new chromophoric system, and that there are no possibilities of extended conjugation across the carbon-carbon bond connecting the two benzanthronyl residues because of the steric hindrance of the hydrogen atoms in the 4,4′- or 3,3′-positions[9].



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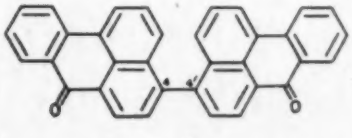
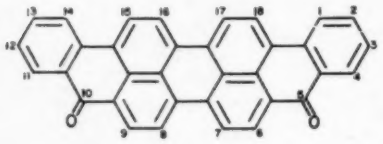


(IV)

The absorption spectrum of 16,17-dimethoxydibenzanthrone (Caledon Jade Green; VI), a dye of outstanding technical importance, in comparison with that of dibenzanthrone (V) was first discussed in connection with the substantivity for cellulose of the leuco derivatives of anthraquinonoid vat dyes in alkaline solution[10]. Attention was drawn to the overlap of the van der Waals radii of the methoxyl groups; the bathochromic shift in passing from dibenzanthrone (V) to the 16,17-dimethoxy derivative (VI) was explained by assuming a planar configuration for the two methoxyl groups and the dibenzanthrone system by adjustments in bond lengths and bond angles.



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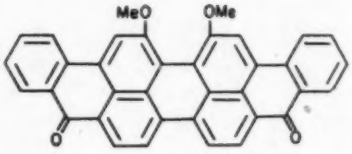
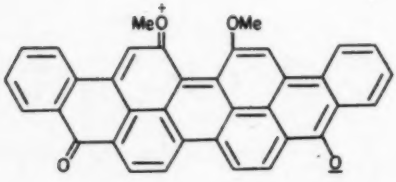


(VI)

A revised scale drawing of (VI), using bond lengths and bond angles varying within the limits indicated by the actual values for perylene [11], shows that a planar configuration is possible in which the overlap of the van der Waals radii of the methoxyl groups is relatively small[12]. Further, the van der Waals radii of the ethereal oxygen atoms will be reduced by resonance with the carbonyl groups as shown in (VII). Since the additional energy required for achieving planarity decreases the resonance energy, the energy of the ground state is raised from its normal level and 16,17-dimethoxydibenzanthrone therefore absorbs at longer wave length than dibenzanthrone. The intensity of the long wave length band of 16,17-dimethoxydibenzanthrone is much lower than that of dibenzanthrone because of the lowering of the probability of the transition from the ground state to the excited state in the strained molecule.



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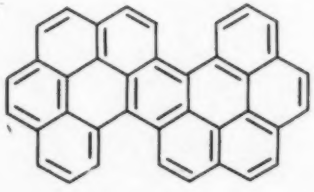
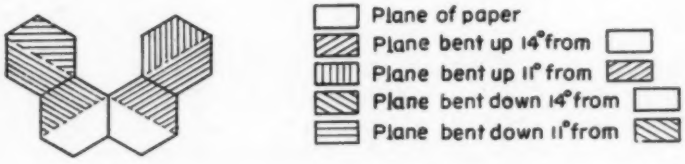


(VIII)

Durie and Shannon[13] have determined in chlorobenzene and dioxane solution the electronic absorption spectra of dibenzanthrone (V), 16,17-dimethoxydibenzanthrone (VI), and other dibenzanthrone derivatives. They found that their curves for (V) and (VI) were similar to those presented by Padhye *et al*[9]., who used *o*-chlorophenol as solvent, and differed considerably in the positions of the peaks as well as the intensities from the data of Moran and Stonehill[14], who determined the absorption spectra in ethanol and chlorobenzene. We have noticed discrepancies between our results and those of Moran and Stonehill for other vat dyes. As suggested by Durie and Shannon, it appears likely that Moran and Stonehill failed to obtain complete solution because of the extremely low solubility of (V) and (VI) in both ethanol and chlorobenzene.

Durie and Shannon considered that the argument concerning the colour of (VI) based on the coplanarity of the methoxyl groups and the polycyclic system was invalidated by the proved non-planarity of molecules such as (VIII). An overcrowded molecule, such as (VIII), in which the repulsion forces between non-bonded carbon atoms situated less than 3.0 Å produce distortions from a planar arrangement as shown in (IX) for 1,2-benzophenanthrene, is, however, very different from (VI) in which the strain is accommodated by a slight deformation in the angles of the bonds linking the ethereal oxygen atoms to the carbon skeleton and by the stretching and compression of bond lengths in the dibenzanthrone system. Because of the single-bond character of the two carbon-carbon bonds uniting the two benzanthrone moieties, Durie and Shannon visualized a twisting of the molecule around an axis of the central ring. This kind of puckering has no parallel in available X-ray data on strained ring systems and is extremely unlikely.



(IX)

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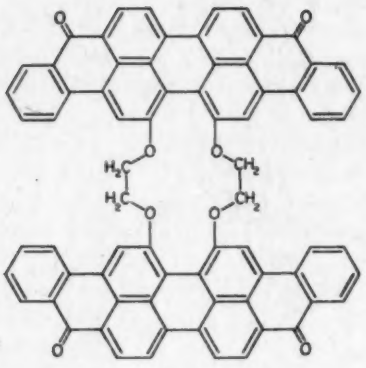
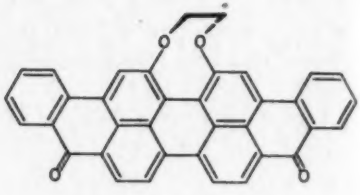
The ethylene ether of 16,17-dihydroxydibenzanthrone is blue in colour and is a commercial dye (Indanthrene Navy Blue G; C.I. 71200). It is prepared by the action of ethylene dibromide or 2-chloroethyl *p*-toluenesulphonate on 16,17-dihydroxydibenzanthrone. The dimeric structure (X) assigned to it earlier[15] should be replaced by the monomeric structure (XI) in the light of the following considerations. The 16-member heterocyclic ring system in (X) involves no additional strain and the ether linkages should be able to adopt the preferred geometry as in (VI); the ethylene ether should therefore be more or less similar in colour to the dimethyl ether (VI). In the monomeric structure (XI), the lone pair orbitals of the oxygen atoms will be rotated away from the direction perpendicular to the mean molecular plane and participation of the lone pair electrons in the resonance of the aromatic system will be greatly reduced. In (XI) a *cis* configuration is shown for the ethylene bridge, but the more probable *trans* configuration, in which one carbon atom is above and one below the plane of the aromatic framework, will not affect the discussion concerning the monomeric character of the ethylene ether. The ethylene ether therefore will absorb at much shorter wave length than the dimethyl ether and will not be expected to be substantially different in colour from the parent dibenzanthrone. The I.G. prepared polymethylene ethers of 16,17-dihydroxydibenzanthrone and observed that when the methylene groups were increased from 2 in Navy Blue G to 3, 4, and 6, the colour changed progressively to green-blue, blue-green, and dull green[16]. If Indanthrene Navy Blue G had the dimeric structure (X), increase in the number of methylene groups should produce little or no alteration in colour; but in the monomeric structure (XI), the strain in the heterocyclic ring will be progressively reduced as the number of methylene groups is increased, and ultimately the ethereal oxygen atoms will be able to take up positions in which they can enter into resonance interaction with the dibenzanthrone system, resulting in a bathochromic shift as in (VI).



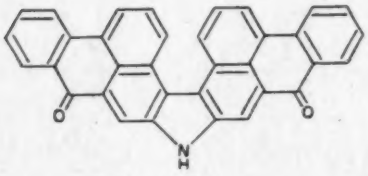
(X)



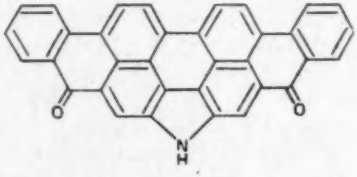
(XI)

The only 5-substituted benzanthrone derivative, to which a reference could be found in the older literature, was 5-nitrobenzanthrone, prepared by Boyes, Grieve, and Rule[17] by a tedious route. 5-Nitrobenzanthrone was subsequently synthesized[18] by taking advantage of the powerful directing influence of the acetamido group in 4-acetamidobenzanthrone; 5-amino-, 5-hydroxy-, and 5-methoxybenzanthrone were then prepared by conventional methods[19]. 7,8-Dimethoxydibenzanthrone, which dyed cotton a greenish blue with very good fastness properties, was prepared by alkali fusion of 5-methoxybenzanthrone and also by alkali fusion of 5-hydroxybenzanthrone, followed by methylation.

5,5′-Dinitro-4,4′-dibenzanthronyl was prepared from 4-amino-5-nitrobenzanthrone through 4-iodo-5-nitrobenzanthrone. Reduction with sodium sulphide yielded 5,5′-diamino-4,4′-dibenzanthronyl and reduction with zinc dust in acetic acid, using the conditions under which Vesely[20] prepared 1,2-7,8-dibenzocarbazole from 1,1′-dinitro-2,2′-dinaphthyl, gave the carbazole (XII). The carbazole (XII) could not be cyclized to the corresponding dibenzanthrone (XIII), which is the structure assigned by Kunz[21] to Indanthrene Grey 3B, prepared by the action of hydroxylamine and sulphuric acid on dibenzanthrone (C.I. 59855). By alkali fusion or treatment with sulphuric acid under suitable conditions 4,4′-dibenzanthronyl (IV) can be cyclized to dibenzanthrone; because of the freedom of rotation about the 4,4′-bond, the 3,3′-carbon atoms come close enough for the elimination of two hydrogen atoms with the formation of the stable dibenzanthrone system.



(XII)

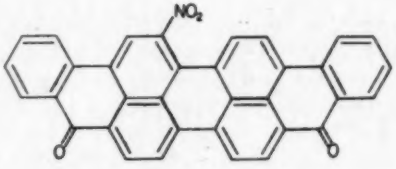


(XIII)

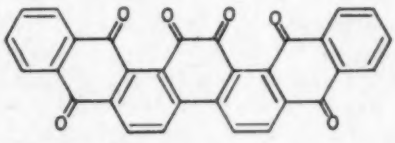
Nitration of Dibenzanthrone

Nitration of dibenzanthrone in acetic acid, chloracetic acid, or nitrobenzene at about 25° gives a mixture of nitrodibenzanthrones, which dye cotton an unlevel green of no practical value. Since the nitro groups are reduced during vatting, the product on the fibre is a mixture of aminodibenzanthrones. When the green dye is oxidized on the fibre with sodium hypochlorite, a deep

black shade is produced, and nitrated dibenzanthrone (C.I. 59850) is marketed under the names of Indanthrene Black BB and BGA, Cibanone Black 2B, Caledon Black NB, etc. Maki[22] considered that nitration yielded mainly 16,17-dinitrodibenzanthrone. Ruling out the Maki structure by somewhat equivocal experimental evidence, Bennett, Pritchard, and Simonsen[23] placed the nitro groups in the 3,12-positions by analogy with disubstitution in benzanthrone where the second substituent enters the 9-position, which corresponds to the 3- or 12-position in dibenzanthrone. This orientation was disproved[24] by the unambiguous synthesis of 3,12-diaminodibenzanthrone, which dyed a dull green shade turning bright blue after hypochlorite oxidation. The constitution of the essential constituent of nitrated dibenzanthrone has now been conclusively proved to be 16-nitrodibenzanthrone (XIV). Crystalline 16-nitrodibenzanthrone (XIV) was prepared by nitration of dibenzanthrone and also isolated from the commercial product by chromatography on alumina[25] at 110°. Chromic acid oxidation, followed by decarboxylation, gave 2,2′-dianthraquinonyl. The constitution was confirmed by reduction to 16-aminodibenzanthrone, synthesized by alkali fusion of an equimolar mixture of benzanthrone and 2-aminobenzanthrone; the resultant mixture of dibenzanthrone, 16-aminodibenzanthrone, and 16,17-diaminodibenzanthrone was separated by hot chromatography. 16,17-Diaminodibenzanthrone was also prepared by alkali fusion of 2-aminobenzanthrone. Oxidation of 16-nitrodibenzanthrone or 16,17-dimethoxydibenzanthrone with chromic and sulphuric acids under controlled conditions gave 1,2,7,8-diphthaloylphenanthraquinone (XV), a new triquinone; further oxidation then yielded the known 2,2′-dianthraquinonyl-1,1′-dicarboxylic acid. Oxidation of 16,17-diaminodibenzanthrone with sodium hypochlorite gave a product which may have the pyridazine structure assigned by Maki to the black dye produced on the fibre by means of Indanthrene Black BB; but it dyed a brown shade, unaffected by chlorine, from a blue vat.



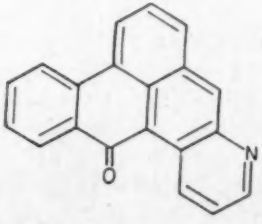
(XIV)



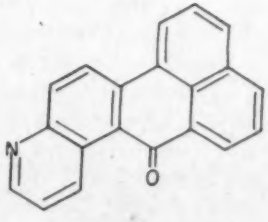
(XV)

The Constitution of Bally's "Benzanthronequinoline" and of Cyananthrene

By the action of glycerol and sulphuric acid on 2-aminoanthraquinone in the absence of an oxidizing agent, Bally (1905) obtained as the major product a "benzanthronequinoline" to which he assigned the structure (XVI). The correct structure was shown many years later to be (XVII) since Bally's compound was identical with the product of the Skraup reaction on 9-aminobenzanthrone[26].



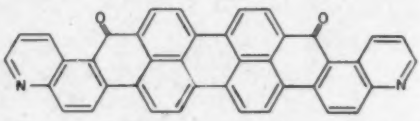
(XVI)



(XVII)

Cyananthrene (Cyananthrone; Indanthrene Dark Blue BT; C.I. 68705; Bally and Isler, 1904), prepared by alkali fusion of Bally's benzanthronequinoline (XVII), is no longer used commercially. By analogy with the formation of dibenzanthrone from benzanthrone, but without a re-examination of the preparation and properties of cyananthrene, the structure (XVIII) was assigned to cyananthrene[26]. Bradley and Sutcliffe[27] repeated the preparation of cyananthrene with a slight modification of Bally's conditions and submitted the crude black product to a process of purification, involving extraction with 1,2,4-trichlorobenzene and phenol and hot chromatography of the soluble fraction. A minute amount of a dye was thus isolated, which exhibited in concentrated sulphuric acid solution an absorption spectrum corresponding to an isodibenzanthrone and not to a dibenzanthrone derivative. They then concluded that cyananthrene had the isodibenzanthrone structure (XIX). The presence of (XVIII) in cyananthrene was not excluded by Bradley and Sutcliffe's work, which only provided evidence of the fact that crude cyananthrene contains a substance which probably has the isodibenzanthrone structure (XIX).

(XIX)



(XVIII)

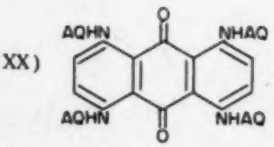
The spectrum of the cyananthrene fraction, recorded by Bradley and Sutcliffe, shows the characteristics of dibenzanthrone beyond 780 mμ. Unni[28] determined the spectrum of an equimolecular mixture of dibenzanthrone and isodibenzanthrone in sulphuric acid, which indicated that cyananthrene is a mixture of at least two dyes having the dibenzanthrone and the isodibenzanthrone structures. Through the courtesy of Farbenfabriken Bayer an authentic sample of Cyananthrene 0 was obtained and examined. It contained 14% of acetone-soluble substances; chromatography of a benzene solution on alumina led to 4(*N*), 5-pyridinobenzanthrone, 1-azanaphthacene-6,11-dione, 2-aminoanthraquinone, and several unidentified fractions. The residual dye was a mixture of vattable (47%) and unvattable (35%) fractions, neither of which could be crystallized. Both gave similar colour reactions, but the absorption spectra in sulphuric acid were different in the region beyond 770 mμ. The spectrum of the vattable portion showed an absorption maximum at 880 mμ; the spectrum of dibenzanthrone in sulphuric acid has a peak at 848 mμ, while isodibenzanthrone shows no absorption beyond 790 mμ. The available evidence therefore indicates that cyananthrene contains the dipyridino derivatives (XVIII and XIX) of both dibenzanthrone and isodibenzanthrone.

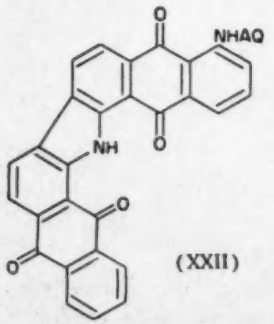
According to Akamatu and Inokuchi[29], cyananthrone "has the highest conductivity so far known among the single organic compounds. Its conductivity is almost comparable to that of selenium, which is a typical inorganic semiconductor". The source form which cyananthrone was obtained has not been specified, but the structure (XVIII) is mentioned. "Indanthrene Black", to which Maki's erroneous azine structure is assigned, is also stated to have high conductivity. In view of the interesting semiconductor properties of cyananthrene, attempts are now being made to synthesize the pure dyes with the authentic structures (XVIII) and (XIX). Bradley and Sutcliffe attempted to prepare (XVIII) by the action of copper on the 3-bromo derivative of (XVII), but the only isolable product was the debrominated pyridinobenzanthrone (XVII) or a black insoluble substance, considered to be probably a complex pyridinium salt.

Anthrimides and Carbazoles

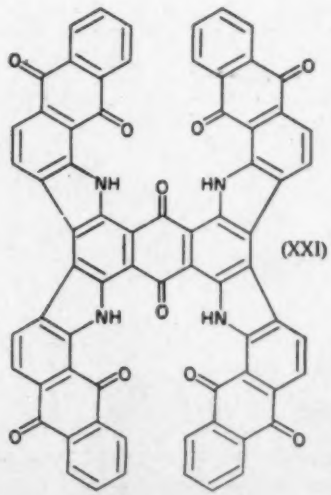
When 1,1′-dianthraquinonylamine (1,1′-anthrimide) is heated with aluminium chloride, cyclization to a carbazole takes place; several carbazole derivatives of this type are largely used vat dyes of yellow, orange, khaki, brown, and olive shades. Vigorous treatment with an oxidizing agent, such as sodium hypochlorite, is essential for the development of the pure shade. The mechanism of the reactions has not been fully elucidated and the structures assigned to some of the dyes are plausible, rather than conclusively proved[30]. An example is Indanthrene Khaki GG (C.I. 71050), prepared by condensing one molecule of 1,4,5,8-tetrachloroanthraquinone with four molecules of 1-aminoanthraquinone and heating the pentanthrimide (XX; AQ=1-anthraquinonyl) with aluminium chloride. The tetracarbazole structure (XXI) is usually assumed, but there has been some doubt if all the four anthrimide groups undergo cyclization. Jayaraman[31] carried out extensive work on this problem; his results indicate that Khaki GG very probably possesses the tetracarbazole structure (XXI). Jayaraman synthesized and examined a series of anthrimides, corresponding carbazoles, and compounds (such as XXII) containing both anthrimide and carbazole groups. Oxidation and reduction experiments, absorption spectra in organic solvents, and absorption spectra of the leuco derivatives in alkaline solution did not throw any new light on the structure of Khaki GG; the simpler anthrimides and carbazoles could be distinguished on the basis of their absorption spectra in organic solvents, but Khaki GG was almost totally insoluble. The absorption spectra in sulphuric acid supported the tetracarbazole structure (XXI). Anthrimides showed two peaks at about 263 mμ and 360 mμ; the carbazoles exhibited a peak at about 260 mμ and a broad band at about 508 mμ; compounds (such as XXII) containing both anthrimide and carbazole groups exhibited absorption bands in all the three regions. Khaki GG in sulphuric acid showed absorption maxima at about 260 mμ and 540 mμ, and the anthrimide peak at 360 mμ was absent. Infrared spectra also supported the tetracarbazole structure (XXI)[32]. The NH groups in the anthrimides are involved in strong hydrogen bonding with the neighbouring carbonyl groups, and all the anthrimides including anthrimidecarbazoles (XXII) showed two strong bands at 1670-1664 and 1665-1630 cm^{-1}. In the carbonyl region the carbazoles including Khaki GG showed only one band at about 1666 cm^{-1}.

(XX)





(XXII)

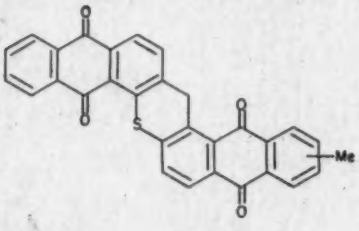


(XXI)

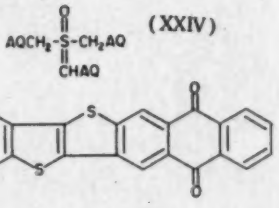
Bradley and Pandit[33] synthesized a compound, which they believed to be the tetracarbazole (XXI), but by a series of reactions which gave amorphous intermediate products and which in fact provided no evidence concerning the structure of their ultimate product. Since their final product dyed a yellowish shade on cotton, it was presumably different from Khaki GG, although this conclusion was not specifically stated.

Cibanone Yellow R and Orange R

By fusing 2-chloromethylanthraquinone or its chloro derivatives with sulphur and treating the product with sodium hypochlorite, a bright orange-yellow dye (Cibanone Yellow R; C.I. 69705; Mayer and Schaarschmidt, 1908) is obtained[34]. Thionation of the same intermediates at a higher temperature gives Cibanone Orange R (C.I. 69700). Both these dyes were withdrawn from the commercial range of Cibanone colours because of their degradative effect on cellulose when the dyed material was exposed to light. This photochemical activity of Cibanone Yellow R and Orange R is indeed so marked that they have been the dyes of choice for investigating the accelerated oxidation of cellulose by the action of light. Fierz-David and Geering (1935) assigned to Cibanone Yellow R the structure (XXIII) and they regarded Orange R as a polymer related to Yellow R in the same way as Primuline to dehydrothiotoluidine. A re-examination of the chemistry of Cibanone Yellow R and Orange R[35] showed the improbability of the Fierz-David structures. It was found that Yellow R, purified by Fierz-David's method, contained anthraflavone (AQCH=CHAQ; AQ=2-anthraquinonyl), and various considerations led to the structure (XXIV) for Yellow R and (XXV) for Orange R.



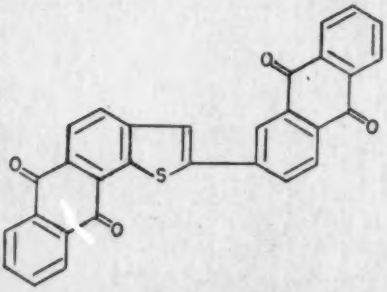
(XXIII)



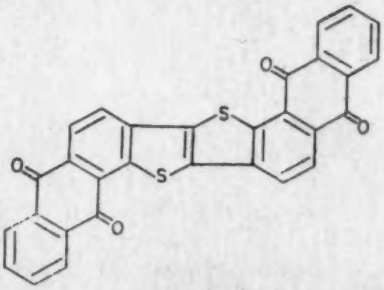
(XXIV)

(XXV)

More recent work[36] has, however, shown that the main tinctorial constituent of Yellow R has the structure (XXVI) and Orange R the structure (XXVII).



(XXVI)

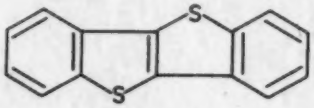


(XXVII)

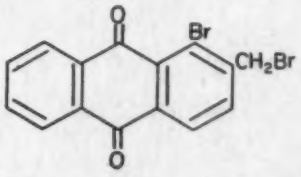
More intensive hot chromatography of the earlier sample of Yellow R on alumina resulted in the separation of a further quantity of anthraflavone and isolation of a major constituent, analysis

of which fits two methylanthraquinone residues per atom of sulphur. Raney nickel desulphurization gave products very similar to those obtained from anthraflavone, and thionation of anthraflavone under appropriate conditions yielded yellow and orange dyes, similar in their properties to Yellow R and Orange R. It was also possible to convert Yellow R by further thionation to Orange R.

Dibenzthiophthene (XXVIII), obtained by Anschutz (1914) in 3% yield by the distillation of *S*-acetylthiosalicylic acid and by Baker[37] in 16% yield by heating thiosalicylic acid with phosphorus pentoxide in tetralin, can be prepared in 50% yield by thionation of *o*-chlorobenzyl bromide at 240-80°. Thionation of 1-bromo-2-bromomethylanthraquinone (XXIX) yielded an orange dye, very similar in all its properties to pure crystalline Orange R. Condensation of (XXVIII) with phthalic anhydride in a melt of aluminium chloride and sodium chloride, or in acetylene tetrachloride in presence of aluminium chloride followed by cyclization with sulphuric acid, yielded a mixture of products, which contained (XXVII) as well as its isomers. The presence of the linear and other isomers in Orange R and Yellow R as minor constituents cannot be excluded.



(XXVIII)

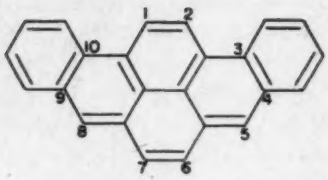


(XXIX)

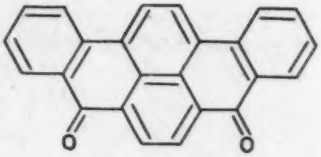
In a review of the photochemical degradation of cellulose, dyed with yellow and orange vat dyes, the stability of semiquinone radicals was suggested as an important factor[38]. The photochemical activity of anthraquinonoid vat dyes has recently been investigated by Bridge[39] using flash photolysis[40]. Bridge has found that semiquinone radicals are present and are stable when formed in deoxygenated irradiated solutions, and he has stated that it is not obvious why such stability (observed in the absence of oxygen) should confer activity on a dye. Several other factors undoubtedly have to be considered, and some work on the chemical constitution of the active vat dyes is now in progress. Bridge has arrived at the conclusion that there is no single comprehensive answer to the tendering problem, but that as soon as a full knowledge of the electronic transitions and of the immediate primary products is obtained, a final answer may be found.

Reduction of Quinones to Hydrocarbons

Applications of Raney nickel reduction and desulphurization to thioindigoid and anthraquinonoid vat dyes have been reviewed elsewhere[41]. The aromatic polycyclic hydrocarbons and their heterocyclic analogues are of interest for their carcinogenic and other physiological properties, chemical reactivity, electronic structure, and absorption spectra. Since many polycyclic quinones are available as commercial anthraquinonoid vat dyes and others are accessible by known synthetic reactions, it is useful to have a variety of methods for the reduction of polycyclic quinones to the corresponding hydrocarbon derivatives. A well-known general method is the Clar reduction by means of zinc dust, zinc chloride, and sodium chloride[42]. Coffey[43] showed that anthraquinone, anthanthrone, and flavanthrone underwent smooth reduction to the corresponding hydrocarbons by treatment with aluminium cyclohexoxide in cyclohexanol. 3,4,9,10-Dibenzopyrene (XXX), a powerful carcinogen, can be prepared from the 5,8-quinone (XXXI) by the Clar reduction, Coffey's application of the Meerwein-Ponndorf reduction, or Raney nickel reduction of the sulphuric ester of the leuco compound.



(XXX)



(XXXI)

Another general method for the reduction of anthraquinone derivatives to anthracene derivatives is treatment with sodium borohydride and boron trifluoride-etherate[44]. The mechanism of this reaction and its limitations are under investigation. In the reduction of anthraquinone, anthracene is accompanied by 9,10-dihydroanthracene, but an overall yield of 70% of anthracene is obtained by aromatization using palladium-charcoal in boiling *p*-cymene[45].

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Reactive Methylene Compounds. Part VII. Condensations with Benzenediazonium Salts

H. G. Garg*

Several benzeneazo derivatives have been synthesised by coupling aromatic diazonium salts with 3,4-dichloro- and 2-chloro-5-methylbenzoyl-acetones, ω-anisoylacetophenone, and ω-benzoyl-3,4-dichloroacetophenone.

In previous communications of this series (Garg and Joshi, this *Journal*, 1960, **37**, 626; Garg, *ibid.*, 1961, **38**, 113, 115), syntheses of the so-called benzeneazo derivatives of β-keto-esters and β-diketones were reported. The present communication describes the preparation of some more compounds. These are obtained by coupling of aromatic diazonium salts with reactive methylene compounds, such as, 3,4-dichloro-, 2-chloro-5-methylbenzoylacetones, ω-anisoylacetophenone, and ω-benzoyl-3.4-dichloroacetophenone.

All these compounds are highly coloured, crystalline solids. These are crystallised from glacial acetic acid.

EXPERIMENTAL**

3,4-Dichlorobenzoylacetone.—Sodium ethoxide (obtained from sodium, 2.3 g. and ethanol, 12 c.c.) was treated with ethyl acetate (40 c.c.). 3,4-Dichloroacetophenone (0.1*M*) was added to the mixture, surrounded by ice, and left overnight. The reaction mixture was poured into ice water. The sodium salt of 3,4-dichlorobenzoylacetone separating was filtered and dried. The solid on acidification gave 3,4-dichlorobenzoylacetone. It was crystallised from ethanol in pale yellow solid, m.p. 84°, yield 52%. (Found : Cl, 30.62. $C_{10}H_8O_2Cl_2$ requires Cl, 30.73%).

2-Chloro-5-methylbenzoylacetone was similarly prepared by taking 2-chloro-5-methylacetophenone. It was crystallised from ethanol in colorless needles, m.p. 61°, yield 54%. (Found : Cl, 16.84. $C_{11}H_{11}O_2Cl$ requires Cl, 16.86%).

ω-Benzoyl-3,4-dichloroacetophenone.—The synthesis was effected by the action of sodium methoxide on dibromide of benzylidene-3,4-dichloroacetophenone. It was crystallised from ethanol in light yellow crystals, m.p. 122°, yield 79%. (Found : Cl, 24.51. $C_{15}H_{10}O_2Cl_2$ requires Cl, 24.23%).

ω-Anisoylacetophenone was prepared by a known method (Pond, Maxwell, and Normann, *J. Amer. Chem. Soc.*, 1899, **21**, 966).

Preparation of Benzeneazo Derivatives of β-Diketones

The benzeneazo compounds of substituted benzoylacetone and ω-benzoylacetophenones were obtained by the action of benzenediazonium chlorides on the corresponding β-diketones, as described earlier (*loc. cit.*). Characteristics of benzeneazo-substituted benzoylacetones and ω-benzoylacetophenones are recorded in Tables I and II respectively.

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** Melting points are uncorrected.

TABLE I

No.	Substituted benzeneazo derivative formed.	3,4-Dichlorobenzoylacetone. Yield.	M.P.	Colour.	Formula.	%Halogen. Found.	Calc.	2-Chloro-5-methylbenzoylacetone. Yield.	M.P.	Colour.	Formula.	%Halogen. Found.	Calc.
1.	Benzeneazo	86%	164°	Reddish yellow	$C_{16}H_{12}O_2N_2Cl_2$	20.97	21.19	86%	122°	Yellow	$C_{17}H_{15}O_2N_2Cl$	11.02	11.28
2.	4-Methoxy-	84	152°	Pale yellow	$C_{17}H_{14}O_3N_2Cl_2$	19.03	19.45	84	127°	Golden yellow	$C_{18}H_{17}O_3N_2Cl$	10.13	10.30
3.	4-Bromo-	92	140°	Light yellow	$C_{16}H_{11}O_2N_2BrCl_2$	36.17	36.47	92	142°	Canary yellow	$C_{17}H_{14}O_2N_2BrCl$	28.97	29.35
4.	4-Chloro-	91	144°	Brownish ,,	$C_{16}H_{11}O_2N_2Cl_3$	28.49	28.82	91	134°	Yellow	$C_{17}H_{14}O_2N_2Cl_2$	20.11	20.34
5.	3-Chloro-	..	..	..	..	..	..	91	128°	Yellow	$C_{17}H_{14}O_2N_2Cl_2$	20.21	20.34
6.	2-Chloro-	90	147°	Orange	$C_{16}H_{11}O_2N_2Cl_3$	28.52	28.82	90	136°	Light yellow	$C_{17}H_{14}O_2N_2Cl_2$	19.93	20.34
7.	4-Nitro-	94	156°	Orange-red	$C_{16}H_{11}O_4N_3Cl_2$	18.83	18.68	95	144°	Light orange	$C_{17}H_{14}O_4N_3Cl$	9.59	9.87
8.	3-Nitro-	..	..	..	..	..	..	93	112°	Pale yellow	$C_{17}H_{14}O_4N_3Cl$	9.61	9.87
9.	4-Methyl-	..	..	..	..	..	..	83	106°	Yellow	$C_{18}H_{17}O_2N_2Cl$	10.53	10.80
10.	2-Chloro-4-nitro-	91	152°	Light yellow	$C_{16}H_{10}O_4N_3Cl_3$	25.38	25.69	93	185°	Yellow	$C_{17}H_{13}O_4N_3Cl_2$	17.81	18.02
11.	2-Nitro-4-chloro-	91	184°	Canary yellow	$C_{16}H_{10}O_4N_3Cl_3$	25.41	25.69	92	138°	Golden yellow	$C_{17}H_{13}O_4N_3Cl_2$	17.92	18.02

TABLE II

*No.	ω-Anisoylacetophenone. Yield.	M.P.	Colour.	Formula.	Found.	Calc.	ω-Benzoyl-3,4-dichloroacetophenone. Yield.	M.P.	Colour.	Formula.	%Halogen. Found.	Calc.
1.	84%	142°	Yellow	$C_{23}H_{16}O_3N_2$	N : 7.64	7.82	86%	124°	Brownish yellow	$C_{21}H_{14}O_3N_2Cl_2$	17.79	17.88
2.	..	..	..	..	..	..	..	..	..	..	..	..
3.	88	175°	Golden yellow	$C_{22}H_{17}O_3N_2Br$	Br : 18.09	18.30	90	184°	Yellow	$C_{21}H_{13}O_3N_2BrCl_2$	31.58	31.72
4.	87	166°	Yellow	$C_{22}H_{17}O_3N_2Cl$	Cl : 8.88	9.04	89	164°	Pale yellow	$C_{21}H_{13}O_3N_2Cl_3$	24.52	24.68
5.	86	140°	Golden yellow	$C_{22}H_{17}O_3N_2Cl$	Cl : 8.92	9.04	..	..	..	..	..	..
6.	..	..	..	..	..	..	88	126°	Dirty ,,	$C_{21}H_{13}O_3N_2Cl_3$	24.52	24.68
7.	90	159°	Pale yellow	$C_{22}H_{17}O_5N_3$	N : 10.28	10.42	94	208°	Dirty ,,	$C_{21}H_{13}O_4N_3Cl_2$	15.92	16.06
8.	90	146°	Light yellow	$C_{22}H_{17}O_5N_3$	N : 10.19	10.42	93	166°	Dirty ,,	$C_{21}H_{13}O_4N_3Cl_2$	15.88	16.06
9.	82	170°	Yellow	$C_{23}H_{20}O_3N_2$	N : 7.41	7.52	..	..	..	..	..	..
10.	89	162°	Yellow	$C_{23}H_{16}O_5N_2Cl$	Cl : 7.91	8.11	93	176°	Light ,,	$C_{21}H_{13}O_4N_3Cl_3$	22.18	22.35
11.	88	154°	Golden yellow	$C_{23}H_{16}O_5N_2Cl$	Cl : 7.94	8.11	..	..	..	..	..	..

* The number of benzeneazo derivatives corresponds to those listed in Table I.

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Evaluation of Approximate Atomic Weights

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A semi-empirical equation correlating isotopic mass, its mass number, and atomic number has been made the basis for deriving relations that yield approximate values of atomic weights of 91 elements from helium to uranium from a mere knowledge of the atomic numbers of the elements.

The main nucleons, contributing towards nuclear mass, are the protons and the neutrons. As one examines the Periodic Table, the variations in the ratio of proton and neutron numbers in the nuclei of the elements become evident. It is therefore not very easy to comprehend the approximate atomic weight of an element, barring a few at the start, from a mere knowledge of the atomic number of the element.

Different investigators, such as Born and others, have sought to relate nuclear mass in terms of charge (proton number) and mass number of the nucleus. Consideration of some aspects of "liquid drop model" of nucleus together with other operating influences, e.g., coulombic force of interaction, led Weizsäcker (*Z. Physik*, 1935, **96**, 431; vide also Engler and Green, *Phys. Rev.*, 1953, **91**, 40) to suggest a semi-empirical equation for the mass of a nucleus, viz.,

$$M = m_p Z + m_n (A - Z) - \alpha A + \beta A^{\frac{2}{3}} + \epsilon Z^2 A^{-\frac{1}{3}} + \gamma \left(Z - \frac{A}{2}\right)^2 \Big/ A + \delta \qquad .. \quad (1)$$

where, m_p = mass of proton = 1.008, m_n = mass of neutron = 1.0086, A = mass number of the nucleus, Z = atomic number, and α, β, γ, δ, ϵ are constants; α = 15.04 mamu, β = 14.00 mamu, γ = 83 mamu, ϵ = 0.627 mamu, and $\delta = \pm \frac{0.035}{A^{\frac{1}{2}}}$ mamu or 0. This relation provides fair values of stable isotopic mass provided that A and Z are known. In the present communication, an endeavour has been made to obtain a simplified equation, independent of A terms, that can readily be utilised for approximate atomic weight calculation.

For the stablest nucleus of a given mass number, A, the atomic number Z_A is given by

$$Z_A = \frac{m_n - m_p + \gamma}{2\epsilon A^{-\frac{1}{3}} + 2\gamma A^{-1}}$$

or

$$A = 1.986\, Z_A \left[\frac{\epsilon}{\gamma} A^{\frac{1}{3}} + 1\right] \qquad .. \quad (2)$$

Most of the elements up to uranium (Z=92) exist in isotopic forms with different values of A. To apply equation (2) to these isotopes of different elements, one reasonable assumption is made that for any particular Z-value, the theoretically stablest nucleus, governed by equation (2), corresponds to one or the other of the naturally occurring isotopes. For elements with no isotope, the existing species represents the stablest entity.

Although minimum potential energy is the main criterion for indexing the stablest isotope corresponding to a given Z, other physical properties, such as packing fraction values and relative percentage abundance, it may be pointed out, are also qualitative indicators of the degree of stability. Judging from the stand-points of packing fraction and relative abundance, isotopes with greatest percentage abundance do not appear to have always maximum negative packing fraction values. All the same, if for an element, the mass numbers of such isotopes are considered which contribute most towards and make up together at least 90% of the abundance of the element, this group will assuredly contain the stablest species; an average mass number value A (hypothetical) may then be calculated for this group. The relation (2) will not apply to this average mass

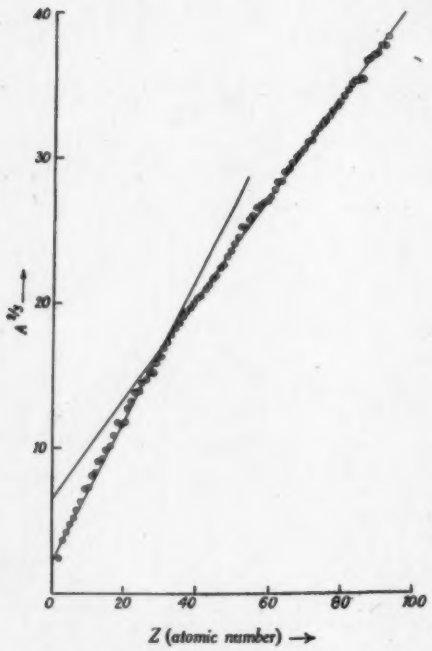
number A. It is assumed that a modified form of equation (2), viz.,

$$A = 1.986\, Z\left[\frac{\epsilon}{\gamma}\, A^{\frac{1}{3}} + 1\right] + \lambda \qquad .. \quad (2a)$$

will apply to the hypothetical average mass number calculated for each element. The deviation expected of A, not representing the mass number of the stablest species, is covered by the term λ, the form of which will be ascertained later. It will be seen afterwards that λ actually possesses two sets of values dependent on Z, the first holding good from helium to zinc and the second, from zinc to uranium. In the above equation, Z_A is deprived of its subscript and replaced by Z for, firstly, all the isotopes of a particular element, whether the stablest or not, have equal proton number and secondly, the additional indication that A in equation (2a) does not represent necessarily the mass number of the stablest isotope.

Hubbard and Meggers ("Periodic Chart of the Atoms", Table IV, p. 31) have compiled a list of stable and longest-lived isotopes of non-radioactive and radioactive elements with their relative percentage occurrence in nature. The data supplied by them have been utilised in evaluating average A and hence of $A^{\frac{1}{3}}$ of elements from He ($Z = 2$) to U ($Z = 92$). A plot of these average $A^{\frac{1}{3}}$ values against corresponding atomic numbers (Z) yields points which fall roughly on two straight lines (Fig. 1) represented by the equations:

FIG. 1



$$A^{\frac{1}{3}} = m_1 Z + c_1 \qquad .. \quad (3a)$$

and

$$A^{\frac{1}{3}} = m_2 Z + c_2 \qquad .. \quad (3b)$$

where, $m_1 = 0.487$, $c_1 = 2.2$, and $m_2 = 0.347$, $c_2 = 6.5$.

One characteristic feature noted in respect of the two straight lines is that elements lying on the decreasing portion and a little beyond of the well-known packing fraction curve lie on the line defined by (3a), *i.e.*, from He to Zn, but those beyond zinc, which lie on the upward rising part of the curve, are governed by equation (3b). The two straight lines intersect on the ordinate corresponding to the abscissa value $Z = 30$.

Now, from (1), omitting δ, which is small, and introducing the values of m_n, α, and A (given by 2a) we have

$$M = \left(1.97\,\frac{\epsilon}{\gamma}Z + \beta\right)A^{\frac{1}{3}} + \epsilon\, Z^2 A^{-\frac{1}{3}} + \gamma\left(Z - \frac{A}{2}\right)^2 \Big/ A + 1.969\, Z + 0.993\,\lambda \qquad .. \quad (4)$$

I. For elements up to $Z = 30$, $\gamma\left(Z - \frac{A}{2}\right)^2 \Big/ A$ is very small and can be neglected. The values of $A^{-\frac{1}{3}}$ for these elements, viz., helium to zinc, vary between the limits 0.629 and 0.248 over an atomic number change of 28 units. These considerations together with (3a) convert (4) into

$$M \simeq (0.0147Z + 0.014))\,(0.487Z + 2.2) + \epsilon Z^2\,\{0.629 + \tfrac{1}{28}\,(2 - Z)\,(0.629 - 0.248)\} + 1.969\,Z + 0.993\,\lambda$$

or $$M = 2.008Z + 7.57 \times 10^{-3} Z^2 - 8.5 \times 10^{-6} Z^3 + 0.031 + 0.993\,\lambda \quad .. \quad (5)$$

The representation of $A^{-\frac{1}{3}}$ by (0.656—0.0136Z) above should not be construed to define a linear dependence of the former on Z. This approximate expression, derivable from actual values, is, in reality, equivalent to $(1.656 - e^{0.0136Z})$, where higher powers of Z, variable from 2 to 30, are reasonably neglected in the exponential expansion. It is seen that a plot of $(1.55 - e^{0.0136Z})$ against Z produces a curve, which closely retraces the one obtained by plotting actual $A^{-\frac{1}{3}}$ values against Z. Since there is hardly any difference of 0.1 between the two expressions, the approximate representation of $A^{-\frac{1}{3}}$ by $(0.656 - 0.0136Z)$ is justified.

The utilisation of the foregoing equation depends on finding out a suitable value for λ. An indirect method of obtaining approximate equivalent to λ consists in comparing the differences between actual atomic weights of a few elements, selected at random (say $Z = 10$, 17, and 30), and those given by $(M - 0.993\,\lambda)$, deducible from equation (5). The differences, equal to $-0.993\,\lambda$, can mostly, within a few tenths of 1 amu, be represented by the expression $0.05 \times (Z - Z_{He})$, Z_{He} being the atomic number of helium, the initial element belonging to curve (1) of Fig. 1. With this value of $0.993\,\lambda$ introduced, equation (5) is converted to

$$M = 1.95Z + 7.57 \times 10^{-3} Z^2 - 8.5 \times 10^{-6} Z^3 + 0.131 \quad .. \quad (6)$$

In deducing equation (6), average mass number A of the elements, existing in different isotopic forms, was considered. Hence M may be taken to represent the atomic weight of the elements. Equation (6) is valid, for reasons already stated, for elements inclusive of and lying between helium and zinc.

II. *For Elements lying between and inclusive of* Zn *and* U

The terms $\epsilon Z^2 A^{-\frac{1}{3}}$ and $\gamma\left(Z - \frac{A}{2}\right)^2 \Big/ A$ occurring in equation (4) vary from element to element. It will be attempted to replace these, in an effort at simplification, by terms independent of A, that on the average will give more or less correct values for these terms.

The value of $A^{-\frac{1}{3}}$ varies from 0.248 for Zn to 0.161 for U. The difference of 0.087 is thus spread over a range of 62 atomic number units ($Z_U = 92$ and $Z_{Zn} = 30$). The approximate substitute for the term $\epsilon Z^2 A^{-\frac{1}{3}}$ will therefore be $\epsilon Z^2\{0.248 + (30 - Z) \times 0.0014\}$.

Similar considerations, when applied to $\gamma\left(Z - \frac{A}{2}\right)^2 \Big/ A$, yield the term $\gamma\,[0.0961 + (Z - 30) \times 0.0478]$ as an approximate equivalent for the latter. These equivalents together with equation (3b) change equation (4) into

$$M = 2.073Z + 5.28 \times 10^{-3} Z^2 - 8.8 \times 10^{-7} Z^3 - 0.02 + 0.993\,\lambda \quad .. \quad (7)$$

It may incidentally be noted that $(0.29 - 0.0014Z)$, the assumed equivalence of $A^{-\frac{1}{3}}$, is what an expansion of $(1.29 - e^{0.0014Z})$ would lead to after proper neglect of small terms for Z values ranging from 30 to 92. The expression $(1.29 - e^{0.0014Z})$ yields values close to the ones actually obtained for $A^{-\frac{1}{3}}$ for any particular Z. The value of 0.993λ in equation (7) can by expressed by a similar term as before, viz., $0.05 \times (Z - Z_{Zn})$, where Z_{Zn} is the atomic number of initial element on the second straight line of Fig. 1. With $0.993\,\lambda = 0.05Z - 1.5$, equation (7) yields

$$M = 2.12Z + 5.28 \times 10^{-3} Z^2 - 8.8 \times 10^{-7} Z^3 - 1.52 \quad .. \quad (8)$$

This equation may be utilised in computing the atomic weights of elements with atomic numbers lying between $Z = 30$ and $Z = 92$, *i.e.*, from zinc to uranium.

Before examining the applicability of equations (6) and (8) to different elements, it will be worthwhile to consider the conditions under which these were derived.

(1) The use of an average A value for an element, though it may not have any physical significance.

(2) Equation (2), when modified by introduction of an additional term λ, applies to these average A values.

(3) Substitution of terms $A^{-\frac{1}{3}}$ and $\left(Z-\frac{A}{2}\right)^2 \Big/ A$ by average terms involving Z only.

Working within the framework of these limitations, the expected results by the application of equations (6) and (8) should only be approximate. Nevertheless, it is interesting to examine the extent of accuracy when the two equations are appropriately applied over the entire range of 91 elements. The following table summarises the results.

TABLE I

Range of accuracy.	Atomic numbers of the elements.	Total.
Within 1 amu of real atomic weight	2 to 15, 17, 19, 21, 24, 26, 27, 29 to 33, 35, 37 to 40, 42 to 44, 46, 48, 49, 59 to 63, 65, 67 to 78, 87, 88, 90, 92.	61
Within 2 amu of real atomic weight	16, 20, 22, 23,25, 28, 36, 41, 45, 47 50, 51, 53, 55, 58, 64, 66, 79, 83, 89.	20
Within 3 amu of real atomic weight	18, 34, 57, 86, 54.	5
Beyond 3 amu of real atomic weight	52, 56, 84, 85, 91.	5

A glance at the table will reveal that barring five elements, the atomic weights of 86 elements can roughly be estimated by either equation (6) or (8). Of these, for as many as 61 elements the values lie within 1 unit of real atomic weight, and for 20 elements, within 2 units. The values afforded by these equations are too approximate to be of any practical utility. Nevertheless, it is seen that atomic weights can be expressed, with a fair measure of accuracy, as a function of atomic number only.

The cases of appreciable deviations (two bottom columns of Table I, where error exceeds 2 amu) are mostly covered by the following categories :

(1) The so-called misfits in the Periodic Table, viz., A, Te, Pa.

(2) The rare gas members, viz., A, Xe, Rn (of these argon comes under category 1 also).

(3) The sulphur analogues, viz., Se, Te, Po (of these Te also appears in 1).

Three stray elements, vanadium, barium, and lanthanum, fall outside the categories and yet exhibit deviations exceeding 2 amu.

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Isoquinoline Derivatives. Part IX

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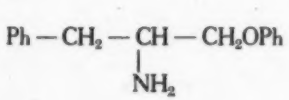
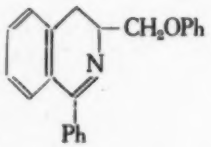
Treatment of the oxime of 1-phenyl-3-phenoxypropan-2-one with sodium and ethanol affords 1-phenyl-2-aminopropane. 1-Phenyl-3-phenoxymethyl-3,4-dihydroisoquinoline and the corresponding 3-hydroxymethyl derivative, 3-piperidinocarbonyl-, 3-piperidinomethyl-, 3-benzyl-3,4-dihydro-, 3-benzyl-, and 3-(α-1-piperidylbenzyl)-isoquinolines have been synthesised.

One of the major drawbacks of papaverine and related synthetic isoquinoline antispasmodics is their weakly basic character. The salts are easily hydrolysed producing acidic reaction, which causes pain at the site of injection. To obviate this difficulty it has been considered desirable to introduce further basic groups in the isoquinoline ring with substituents which may be expected to promote activity. In fact, the introduction of a 3-pyridyl group in 1-position of 3-methyl-6,7-methylenedioxyisoquinoline has furnished a compound much more active than papaverine (Merck, G.P., 613,005/1935).

Based on the observation that 3-methylisoquinolines are potent antispasmodics with low toxicity (Kreitmair, *Arch. Exp. Path. Pharm.*, 1932, **164,** 509; Sugaswa and Sugimito, *J. Pharm. Soc., Japan*, 1941, **61,** 62) and that replacement of the benzyl group in 1-position of papaverine type of compounds by phenyl increases activity, it has been considered desirable to introduce basically substituted methyl group in 3-position of 1-phenylisoquinoline derivatives. As an approach to the problem, the reduction of the oxime of 1-phenyl-3-phenoxypropan-2-one (Pfeiffer and Epler, *Annalen*, 1940, **545,** 263) has been attempted with sodium and ethanol, when 1-phenyl-2-aminopropane has been obtained, obviously through the reductive fission of the arromatic ether group. Similar observations on the fission of aromatic ethers by the action of sodium in refluxing pyridine have been recorded (Prey, *Ber.*, 1943, **76B,** 156). 1-Phenyl-3-phenoxy-2-aminopropane (I) has been prepared by hydrolysis of the Leuckart reaction product from 1-phenyl-3-phenoxypropan-2-one. The benzoyl derivative of (I), when subjected to the Bischler-Napieralski cyclisation, has afforded 1-phenyl-3-phenoxymethyl-3,4-dihydroisoquinoline (II), which after dehydrogenation has been treated with hydrobromic acid to yield the 3-hydroxymethyl derivative (III). The low yields of the products in these stages, specially in the Leuckart reaction, stood in the way of further progress.



(I)



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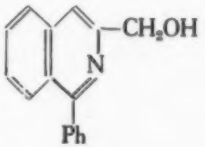
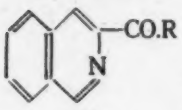


(III)

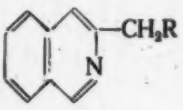
As a further approach to the problem, ethyl isoquinoline-3-carboxylate (Clemo and Hoggarth, *J. Chem. Soc.*, 1954, 95) has been condensed with piperidine to afford 3-piperidinocarbonylisoquinoline (IV), which on reduction with lithium aluminium hydride has yielded 3-piperidinomethylisoquinoline (V).

Papaverine carries a substituted benzyl group at 1-position of the isoquinoline. 3-Benzylisoquinoline has been synthesised to ascertain the effect of a benzyl group at 3-position instead

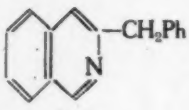
of at 1-position. This compound has been described by Rügheimer (*Annalen*, 1903, **326**, 261; 1903, **328**, 326). He obtained it along with the 4-isomer by treatment of benzoyltetrahydroisoquinoline with benzaldehyde under pressure at 200° and subsequent separation of the isomers. 3-Benzylisoquinoline has now been prepared by an unambiguous method: *N*-Formyl-α-benzyl-β-phenylethylamine (Rajagopalan, *Proc. Ind. Acad. Sci.*, 1941, **14A**, 126; Dey and Ramanathan *Proc. Nat. Inst. Sci., India*, 1943, **9**, 193) has been subjected to the Bischler-Napieralski cyclisation with a mixture of polyphosphoric acid and phosphorus oxychloride to afford 3-benzyl-3, 4-dihydroisoquinoline (VI), which on dehydrogenation with Pd-C has yielded 3-benzylisoquinoline (VII), the physical characteristics of which have been found to be at variance with those described by Rügheimer (*loc. cit.*). The compound (VII) has been brominated and the bromo-derivative treated with piperidine to yield (VIII).



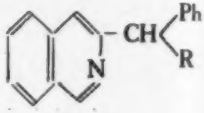
(IV)



(V)



(VII)



(VIII)

[R = piperidino]

The biological activity of the compounds is under study.

EXPERIMENTAL

Oxime of 1-*phenyl-3-phenoxypropane-2-one* was prepared by the interaction of 1-phenyl-3-phenoxypropane-2-one (Pfeiffer and Epler, *loc. cit.*) and hydroxylamine hydrochloride in presence of NaOH. It was recrystallised from ethanol in colorless needles, m.p. 94-96°. (Found: N, 5.74. $C_{15}H_{15}O_2N$ requires N, 5.81%).

Formation of 1-*Phenyl-2-aminopropane.*—Sodium (20 g.) was gradually added to a solution of the preceding oxime (15 g.) in anhydrous ethanol (220 c.c.) and the mixture refluxed till complete dissolution of sodium. It was poured in ice-water and extracted with ether. The ether extract was shaken with HCl (dil.) and the acid solution basified with NaOH. The liberated amine was taken up in ether and dried (K_2CO_3). After removal of the ether, a viscous oil (6 g.) was obtained, which was benzoylated by the Schotten-Baumann method, and the product was recrystallised from dilute ethanol in colorless needles, m.p. 132-33°. (Found: N, 5.79. Calc. for $C_{16}H_{17}ON$: N, 5.86%).

The above benzoyl derivative was identified with an authentic sample (British Pharmacopœia, 1958, p. 43).

1-*Phenyl-3-phenoxy-2-aminopropane* (I).—Formic Acid (98%, 46 g.) was neutralised with ammonium carbonate (46 g.) and the solution was distilled up to 165°. The residue was treated with 1-phenyl-3-phenoxypropane-2-one (30 g.). The mixture after refluxing at 180-90° for 16 hours was hydrolysed by HCl (conc., 100 c.c.) under reflux for 6 hours. The solution was washed with ether, cooled, and basified. The liberated amine was taken up in ether and the extract dried (K_2CO_3). Removal of the ether left the amine as a thick liquid (2 g.), which was characterised as the benzoyl derivative, crystallising from ethanol in colorless needles, m.p. 124-25°. (Found: N, 4.14. $C_{22}H_{21}O_2N$ requires N, 4.23%).

1-*Phenyl-3-phenoxymethyl-3,4-dihydroisoquinoline* (II).—A mixture of 1-phenyl-2-benzamido-3-phenoxypropane (2.5 g.), toluene (30 c.c.) and $POCl_3$ (7 c.c.) was refluxed for 4 hours. Toluene was distilled and the residue was poured into ice-water. The solution was washed with ether and

the acidic aqueous solution was cooled, basified, and extracted with ether. The ether extract was dried. The residue obtained after removal of the solvent was crystallised from petroleum ether (b.p. 40-60°) as brownish plates, m.p. 75-76°. (Found : N, 4.48. $C_{22}H_{19}ON$ requires N, 4.47%).

1-*Phenyl*-3-*hydroxymethylisoquinoline* (III).—The above isoquinoline (II, 1 g.) was dehydrogented by heating at 240-50° for 3 hours in CO_2-atmosphere in presence of Pd-C (10%, 0.25 g.) and tetralin (10 c.c.). After removal of the catalyst the base was extracted with HCl. The acid solution was basified to yield the aromatised isoquinoline as a brownish viscous liquid (0.7 g.), which was characterised as *chloroplatinate*, m.p. 204-206° (decomp.). [Found : N, 3.08 ; Pt, 19.54. $2(C_{22}H_{17}ON).H_2PtCl_6$ requires N, 2.71 ; Pt, 18.9%].

The aromatised isoquinoline (1 g.) was refluxed for 8 hours with constant boiling hydrobromic acid (48%, 20 c.c.). The acid was dustilled, the residue was poured in ice, and the solution was washed with ether. The aqueous solution was filtered, basified with ammonia, extracted with ether, and the ether removed after drying over sodium sulphate. The viscous liquid (0.9 g.) obtained solidified on chilling and scratching. It was crystallised from petroleum ether (b.p. 60-80°) in light cream-coloured plates, m.p. 84-86°. (Found : N, 5.75. $C_{16}H_{13}ON$ requires N, 5.96%).

3-*Piperidinocarbonylisoquinoline* (IV).—A mixture of ethyl isoquinoline-3-carboxylate (Clemo and Hoggarth, *loc. cit.*) (5.5 g.), piperidine (6 c.c.) and diphenyl oxide (50 c.c.) wat refluxed for 10 hours, cooled, and then extracted with HCl (dil.). The acid solution was basified with ammonia and extracted with benzene. The benzene extract was repeatedly washed with water, dried, and distilled to remove the solvent. The residue was distilled when a pale yellow liquid (7 g.), b.p. 210-15°/3-4 mm, was obtained. On chilling it solidified. It was crystallised from petroleum ether (b.p. 60-80°) in colorless plates, m.p. 94-95°. (Found : N, 11.98. $C_{15}H_{16}ON_2$ requires N, 11.67%).

The *picrate* crystallised from ethanol in yellow rectangular plates, m.p. 174-75°. (Found : N, 14.96. $C_{15}H_{16}ON_2.C_6H_3O_7N_3$ requires N, 14.93%).

3-*Piperidinomethylisoquinoline* (V).—To a well-stirred suspension of $LiAlH_4$ (1 g.) in dry ether (250 c.c.) a solution of (IV, 4.5 g.) in dry ether (300 c.c.) was added dropwise at such a rate that the mixture refluxed, when a faint curdy white precipitate separated. The mixture was refluxed for 8 hours, poured in ice, and an aqueous solution of sodium potassium tartrate (20 g.) was added. The ether layer was separated and the aqueous solution extracted with ether. The combined ether solution was shaken with HCl (dil.), basified with ammonia, and then extracted with ether. The ether extract was washed with water and dried (Na_2SO_4). Removal of the ether left a viscous oil (1.5 g.).

The *picrate* crystallised from ethanol in yellow needles, m.p. 174-76°. (Found : C, 47.64 ; H, 3.29 ; N, 16.23. $C_{15}H_{18}N_2$. 2 $C_6H_3O_7N_3$ requires C, 47.36 ; H, 3.51 ; N, 16.37%).

The *chloroplatinate* was obtained as a brown microcrystalline solid, m.p. 242° (decomp.).

3,4-*Dihydro*-3-*benzylisoquinoline* (VI).—A mixture of P_2O_5 (300 g.) and H_3PO_4 (89%, 192 g.) was heated at 100° under stirring in an oil bath for an hour. *N*-Formyl-α-benzyl-β-phenylethylamine (70 g.) was added at room temperature, followed by addition of $POCl_3$ (60 c.c.). The mixture was cautiously heated at 100° with vigorous stirring, when there was much foaming. The temperature was raised to 110° during 3 hours and then kept at 125-30° for 3½ hours. The reaction mixture was then cooled, poured into ice, and the solution was washed with benzene. The aqueous solution was basified with NaOH and thoroughly extracted with benzene. After removal of the benzene the residue was distilled to yield the base (50 g.), b.p. 178-82°/1 mm.

The *picrate* crystallised from ethanol in yellow plates, m.p. 262-63°. (Found : N, 12.32. $C_{16}H_{15}N.C_6H_3O_7N_3$ requires N, 12.44%).

3-Benzylisoquinoline (VII).—A mixture of (VI, 40 g.), Pd-C (10%, 10 g.) and tetralin (350 c.c.) was heated under a current of CO_2 in an oil bath at 240-50° for 5 hours. The mixture was cooled, filtered, and the residue was washed with benzene. The washings and the filtrate were combined and thoroughly extracted with cold HCl (dil.). The acid solution was washed with ether, basified with NaOH, and the separated oil was extracted with benzene. The benzene solution was dried (K_2CO_3) and distilled to remove benzene. The residue was distilled to yield an almost colorless oil (32 g.), b.p. 188-92°/1 mm. (Found : N, 6.22. $C_{16}H_{13}N$ requires N, 6.39%). Rügheimer (*loc. cit.*) recorded b.p. 311°/23 mm and m.p. 104°.

The *picrate* crystallised from ethanol in yellow cottony needles m.p. 181-82°. (Found : N, 12.32. $C_{16}H_{13}N.C_6H_3O_7N_3$ requires N, 12.5%). Rügheimer (*loc. cit.*) recorded m.p. 199°.

The *hydrochloride* was crystallised from absolute ethanol in colorless plates. It does not melt even at 300°. (Found : N, 5.22. $C_{16}H_{13}N.HCl$ requires N, 5.48%).

3-(α-1-Piperidinobenzyl)-isoquinoline (VIII)

(*a*). *3-(α-Bromobenzyl)-isoquinoline Hydrobromide.*—To a solution of 3-benzylisoquinoline (12 g.) in CCl_4 (dry, 125 c.c.) benzoyl peroxide (0.05 g.) was added, followed by a solution of bromine (9 g.) in CCl_4 (dry, 25 c.c.) dropwise under cooling. At first bromine was decolorised very rapidly and gradually a yellowish crystalline precipitate began to form. On further addition of bromine the precipitate turned reddish brown and pasty in nature. The reaction mixture was left overnight at room temperature. CCl_4 was decanted and the residual pasty brownish solid triturated with acetic acid when it became granular in nature. It was filtered, washed with acetic acid, and finally with ether. The yellowish solid (9 g.) was used directly for the next operation.

(*b*). To the above compound (5 g.) piperidine (40 c.c.) was added under cooling. The mixture was refluxed for 5 hours. After removing piperidine by distillation under reduced pressure the residue was treated with water and extracted with ether. The ether extract was repeatedly washed with water and dried (Na_2SO_4). Removal of the ether left a highly viscous base (5 g.).

The *picrate* crystallised from ethanol in yellow needles, m.p. 181-83°. (Found : N, 12.9. $C_{21}H_{22}N_2.C_6H_3O_7N_3$ requires N, 13.2%).

The *phosphate* was recrystallised from methanol as a colorless, microcrystalline powder, m.p. 180-82°. (Found : N, 4.01 ; P, 17.4. $C_{21}H_{22}N_2.4H_3PO_4$ requires N, 4.03 ; P, 17.86%).

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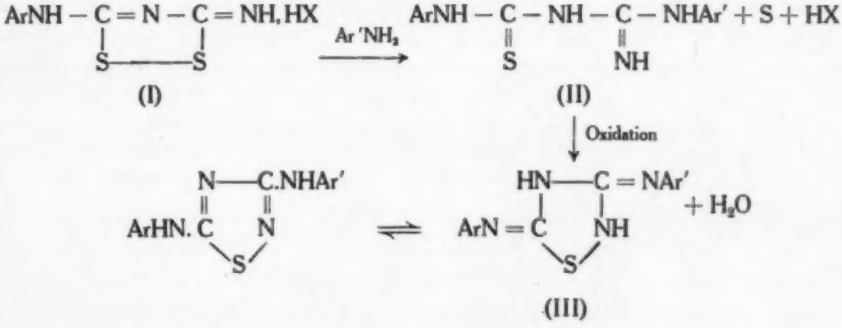
Interaction of Alkyl-substituted Thiurets and Aromatic Amines: Formation of *N*-Arylformamido-*N'*-alkylthiocarbamides and their Oxidation to the Related 3-Arylamino-5-alkylamino-1, 2, 4-thiadiazoles*

S. N. Dixit

Like their aryl homologues the hydrogen halides of the alkyl-substituted thiurets react with the aromatic amines to afford the related *N*-arylformamido-*N'*-alkylthiocarbamides. The structure of these has been confirmed by their preparation by the condensation of appropriate alkyl isothiocyanates with arylguanidines or by the reaction of the related *N'*-alkyl-*N*-cyanothiocarbamide with aromatic amines. The formamidothiocarbamides on oxidation undergo ring closure, forming 3-arylamino-5-alkylamino-1,2,4-thiadiazoles.

The interaction of hydrogen halides of aryl-substituted thiurets (I) and aromatic amines has been shown to afford *N*-arylformamido-*N'*-arylthiccarbamides (II), which when oxidised undergo ring closure to (III), the related 3,5-diarylamino-1,2,4-thiadiazoles or thiadiazolidines (this *Journal*, 1960, **37**, 151).



The above reactions have now been investigated with respect to the following:

(*i*) Methylthiuret hydriodide and aniline, *p*-toluidine, and *p*-phenetidine.

(*ii*) Ethylthiuret hydriodide and *p*-toluidine and *p*-phenetidine.

(*iii*) Dimethylthiuret hydriodide and aniline and *p*-phenetidine.

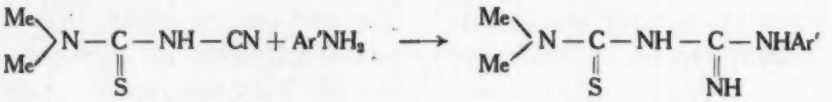
In all cases a thiocarbamide of type (II) (where in place of Ar, the above alkyl groups were substituted) was obtained. The products in the first two cases were identified with the *N*-aryl-formamido-*N'*-alkylthiocarbamides obtained by condensation of the appropriate arylguanidine and alkyl isothiocyanate. Thus:

$$\mathrm{Ar'.NH.C(=NH).NH_2} + \mathrm{R.N:C:S} \rightarrow \mathrm{RNH-C(=S)-NH-C(=NH)-NHAr'}$$

(where Ar' = Ph, *p*-tolyl, and *p*-phenetyl; R = Et and Me).

* In the previous communication (Jan. Issue, 1961, p. 44) in structure (II), double bonded S to be linked to contiguous carbon atoms instead of the N atoms as shown by mistake.

In the case of (*ii*), the product was also identified with the *N*-arylformamido-*N'*-dimethylthiocarbamides, obtained by the interaction of *N'*-dimethyl-*N*-cyanothiocarbamide and aniline or *p*-phenetidine.



(where Ar' = phenyl or *p*-phenetyl).

The above *N*-arylformamido-*N'*-alkyl(or dialkyl)-thiocarbamides, when oxidised with iodine, afforded in all cases the thiadiazoles or thiadiazolidines (III, where Ar is replaced by R which is Me, Et or Me_2).

EXPERIMENTAL

Interaction of Alkyl-substituted Thiuret Hydriodides and Aromatic Amines

Formation of N-*Arylformamido*-N'-*alkylthiocarbamides.*—The required thiuret hydriodide (this *Journal*, 1961, **38**, 44) and the aromatic amine in the molecular proportion of 1:1.5 were heated on a water bath under reflux in ethanolic medium for about 30 minutes. On cooling, the separated sulphur was filtered and the filtrate evaporated to a viscous mass, which solidified on cooling. The unchanged amine and the traces of free sulphur were removed by washing with ether and CS_2. The product was desulphurizable with sodium plumbite solution as was to be expected in the case of compounds (*i*) to (*v*) below, and was found in each case identical with the expected hydriodide of the *N*-arylformamido-*N'*-alkylthiocarbamide. The hydriodides could be recrystallised from hot water or chlorobenzene. The free thiocarbamide was obtained in each case by treatment of the salt with alkali and was crystallised from chlorobenzene. The picrates were prepared by mixing ethanolic solutions of the thiocarbamide and picric acid. The following *N*-arylformamido-*N'* alkylthiocarbamide hydriodides and the related free thiocarbamide bases were obtained.

(*i*) N-*Phenylformamido*-N'-*methylthiocarbamide hydriodide* from methylthiuret hydriodide and aniline, m.p. 158°. (Found : C, 32.14 ; H, 4.05 ; N, 16.95 ; S, 9.85. $C_9H_{13}N_4IS$ requires C, 32.14 ; H, 3.86 ; N, 16.66 ; S, 9.52%). Free thiocarbamide, m.p. 60-61°; picrate, m.p. 177°.

(*ii*) N-p-*Tolylformamido*-N'-*methylthiocarbamide hydriodide* from methylthiuret hydriodide and *p*-toluidine, m.p. 156°. (Found : C, 34.20 ; H, 4.22 ; N, 16.28. $C_{10}H_{15}N_4SI$ requires C, 34.28 ; H, 4.28 ; N, 16.0%). Free thiocarbamide, m.p. 71-72°. (Found : N, 25.38 ; S, 14.32. $C_{10}H_{14}N_4S$ requires N, 25.12 ; S, 14.41%). Picrate, m.p. 193°.

(*iii*) N-p-*Phenetylformamido*-N'-*methylthiocarbamide hydriodide* from methylthiuret hydriodide and *p*-phenetidine, m.p. 184°. (Found : N, 14.77. $C_{11}H_{17}ON_4SI$ requires N, 14.73%). Free thiocarbamide, m.p. 91-92°. (Found : C, 52.66 ; H, 6.42 ; N, 22.16 ; S, 13.03. $C_{11}H_{16}ON_4S$ requires C, 52.38 ; H, 6.34 ; N, 22.22 ; S, 12.69%). Picrate, m.p. 134°.

(*iv*) N-p-*Tolylformamido*-N'-*ethylthiocarbamide hydriodide* from ethylthiuret hydriodide and *p*-toluidine, m.p. 152°. (Found : C, 36.71 ; H, 4.85 ; N, 15.16 ; S, 8.99. $C_{11}H_{17}N_4IS$ requires C, 36.26 ; H, 4.67 ; N, 15.38 ; S, 8.79%). Free thiocarbamide, m.p. 64-65°. Picrate, m.p. 148°.

(*v*) N-p-*Phenetylformamido*-N'-*ethylthiocarbamide hydriodide* from ethylthiuret hydriodide and *p*-phenetidine, m.p. 154°. (Found : N, 14.24. $C_{12}H_{19}ON_4IS$ requires N, 14.21%). Free thiocarbamide, m.p. 101°. (Found : C, 54.26 ; H, 6.72 ; N, 21.02 ; S, 12.43. $C_{12}H_{18}ON_4S$ requires C, 54.13 ; H, 6.76 ; N, 21.05 ; S, 12.03%). Picrate, m.p. 161°.

(*vi*) N-*Phenylformamido*-N′-*dimethylthiocarbamide hydriodide* from dimethylthiuret hydriodide and aniline, m.p. 148°. (Found : N, 15.86. $C_{10}H_{15}N_4S$ requires N, 16.0%). Free thiocarbamide, m.p. 106°. (Found : C, 53.63 ; H, 6.36 ; N, 25.0 ; S, 14.46. $C_{10}H_{14}N_4S$ requires C, 54.05 ; H, 6.30 ; N, 25.22 ; S, 14.41%). This was identified with the product obtained in experiment (*iv*) from *N*′-dimethyl-*N*-cyanothiocarbamide and aniline. Picrate, m.p. 130°.

(*vii*) N-p-*Phenetylformamido*-N′-*dimethylthiocarbamide hydriodide* from dimethylthiuret hydriodide and *p*-phenetidine, m.p. 158°. (Found : N, 14.42. $C_{12}H_{19}ON_4IS$ requires N, 14.21%). Free thiocarbamide, m.p. 94-95°. (Found : C, 54.06 ; H, 6.81 ; N, 21.02 ; S, 12.18. $C_{12}H_{18}ON_4S$ requires C, 54.13 ; H, 6.76 ; N, 21.05 ; S, 12.03%). This was identified with the product obtained in experiment (*iv*) from *N*′-dimethyl-*N*-cyanothiocarbamide and *p*-phenetidine.

Oxidation of N-*Arylformamido*-N′-*alkylthiocarbamides by Iodine*

Formation of 3-*Arylamino*-5-*alkylamino*-1,2,4-*thiadiazoles*.—To the *N*-arylformamido-*N*′-alkylthiocarbamide (about 2 g.), dissolved in ethanol (10 c.c.), aqueous iodine in KI was added gradually with stirring in slight excess. The reaction mixture was cooled and the free thiadiazole bases precipitated by basification with alkali. These were filtered, washed, and crystallised from chlorobenzene in each case. Picrates were prepared by mixing an ethanolic solution of thiadiazoles and picric acid.

(*i*) 3-*Phenylamino*-5-*methylamino*-1,2,4-*thiadiazole* by oxidation of *N*-phenylformamido-*N*′-methylthiocarbamide hydriodide, m.p. 153°. (Found : C, 51.52 ; H, 4.78 ; N, 26.86 ; S, 15.21. $C_9H_{10}N_4S$ requires C, 52.42 ; H, 4.85 ; N, 27.18 ; S, 15.53%). Picrate, m.p. 195°.

(*ii*) 3-p-*Tolylamino*-5-*methylamino*-1,2,4-*thiadiazole* by oxidation of *N*-*p*-tolylformamido-*N*′-methylthiocarbamide hydriodide, m.p. 128°. (Found : C, 55.33 ; H, 5.38 ; N, 25.23 ; S, 15.85. $C_{10}H_{12}N_4S$ requires C, 54.54 ; H, 5.45 ; N, 25.45 ; S, 14.54%). Picrate, m.p. 175°.

(*iii*) 3-p-*Phenetylamino*-5-*methylamino*-1,2,4-*thiadiazole* by oxidation of *N*-*p*-phenetylformamido-*N*′-methylthiocarbamide hydriodide, m.p. 137°. (Found : C, 52.39 ; H, 5.59 ; N, 22.33 ; S, 13.14. $C_{11}H_{14}ON_4S$ requires C, 52.80 ; H, 5.60 ; N, 22.40 ; S, 12.80%). Picrate, m.p. 167°.

(*iv*) 3-p-*Tolylamino*-5-*ethylamino*-1,2,4-*thiadiazole* by oxidation of *N*-*p*-tolylformamido-*N*′-ethylthiocarbamide hydriodide, m.p. 134°. (Found : C, 56.45 ; H, 6.02 ; N, 24.14 ; S, 13.53, $C_{11}H_{14}N_4S$ requires C, 56.41 ; H, 5.98 ; N, 23.93 ; S, 13.67%). Picrate, m.p. 210°.

(*v*) 3-p-*Phenetylamino*-5-*ethylamino*-1,2,4-*thiadiazole* by oxidation of *N*-*p*-phenetylformamido-*N*′-ethylthiocarbamide hydriodide, m.p. 144-45°. (Found : C, 54.23 ; H, 6.02 ; N, 20.98 ; S, 12.46. $C_{12}H_{16}ON_4S$ requires C, 54.54 ; H, 6.06 ; N, 21.21 ; S, 12.12%). Picrate, m.p. 172°.

(*vi*) 3-*Phenylamino*-5-*dimethylamino*-1,2,4-*thiadiazole* by oxidation of *N*-phenylformamido-*N*′-dimethylthiocarbamide hydriodide, m.p. 186-87°. (Found : C, 54.70 ; H, 5.38 ; N, 25.28 ; S, 14.75. $C_{10}H_{12}N_4S$ requires C, 54.54 ; H, 5.45 ; N, 25.45 ; S, 14.54%). Picrate, m.p. 191°.

(*vii*) 3-p-*Phenetylamino*-5-*dimethylamino*-1,2,4-*thiadiazole* by oxidation of *N*-*p*-phenetylformamido-*N*′-dimethylthiocarbamide hydriodide, m.p. 178°. (Found : C, 54.90 ; H, 5.76 ; N, 21.14 ; S, 12.26. $C_{12}H_{16}ON_4S$ requires C, 54.54 ; H, 6.06 ; N, 21.21 ; S, 12.12%). Picrate, m.p. 182°.

Condensation of Monoarylguanidines (carbonates) and Alkyl Isothiocyanates to N-*Arylformamido*-N′-*alkylthiocarbamides and their Oxidation to the Related* 3-*Arylamino*-5-*alkylamino*-1,2,4-*thiadiazoles*

The required monoarylguanidine carbonate and alkyl isothiocyanate (where aryl=phenyl-, *p*-tolyl-, *p*-phenetyl- and alkyl=methyl- and ethyl-) in equimolecular proportions were heated in ethanolic medium under reflux for about 30 minutes. On concentration and cooling, a sticky mass was obtained in each case, which presented difficulties in crystallisation. On crystallisation from ethanol to which some hydriodic acid had been added, crystals of the expected thiocarbamide hydriodide were obtained. Picrates were prepared from ethanolic solution. On oxidation with iodine in ethanol medium, the above obtained *N*-arylformamido-*N′*-alkylthiocarbamide hydriodides gave the related 3-arylamino-5-alkylamino-1,2,4-thiadiazoles. The thiocarbamide hydriodides, their picrates and the thiadiazoles obtained by their oxidation have been identified by undepressed mixed m.p.'s with the respective products described above.

Condensation of N′-*Dimethyl*-N-*cyanothiocarbamide with Aniline and* p-*Phenetidine*

Formation of N-*Phenylformamido- and* N-p-*Phenetylformamido*-N′-*dimethylthiocarbamides and their Oxidation to the Related Thiadiazoles.*—Equimolecular quantities of *N′*-dimethyl-*N*-cyanothiocarbamide and aniline or *p*-phenetidine were heated under reflux in ethanol solution for about 30 minutes. On concentration and cooling, crystals of the expected thiocarbamide separated. Crystallisation was effected with chlorobenzene. On oxidation with iodine in ethanol the related thiadiazoles were formed :

(*a*) N-*Phenylformamido*-N′-*dimethylthiocarbamide*, m.p. 106°. (Found : C, 54.28 ; H, 6.41 ; N, 25.44 ; S, 14.77. $C_{10}H_{14}N_4S$ requires C, 54.05 ; H, 6.30 ; N, 25.22 ; S, 14.41%).

(*b*) 3-*Phenylamino*-5-*dimethylamino*-1,2,4-*thiadiazole* from *N*-phenylformamido-*N′*-dimethylthiocarbamide, m.p. 186-87°. (Found : C, 55.20 ; H, 5.53 ; N, 25.32 ; S, 14.87. $C_{10}H_{12}N_4S$ requires C, 54.54 ; H, 5.45 ; N, 25.45; S, 14.54%).

(*c*) N-p-*Phenetylformamido*-N′-*dimethylthiocarbamide*, m.p. 94-95°. (Found : C, 55.15 ; H, 7.07 ; N, 21.32 ; S, 11.88. $C_{12}H_{18}ON_4S$ requires C, 54.13 ; H, 6.76 ; N, 21.05 ; S, 12.03%).

(*d*) 3-p-*Phenetylamino*-5-*dimethylamino*-1,2,4-*thiadiazole* from *N*-*p*-phenetylformamido-*N′*-dimethylthiocarbamide, m.p. 178°. (Found : C, 54.71 ; H, 6.12 ; N, 21.40 ; S, 12.36. $C_{12}H_{16}ON_4S$ requires C, 54.54 ; H, 6.06 ; N, 21.21 ; S, 12.12%).

These thiocarbamides and thiadiazoles were found identical by undepressed mixed m.p.'s with the corresponding products described above (*vide supra*).

Sincere thanks of the author are to Dr. R. H. Sahasrabudhey for his interest, to Prof. G. B. Singh, and the authorities of the Banaras Hindu University for facilities and to the Ministry of Scientific Research and Cultural Affairs, Government of India, for a scholarship.

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Possible Antiamoebic Agents. Part XIII. Synthesis of Substituted Quinoxalines

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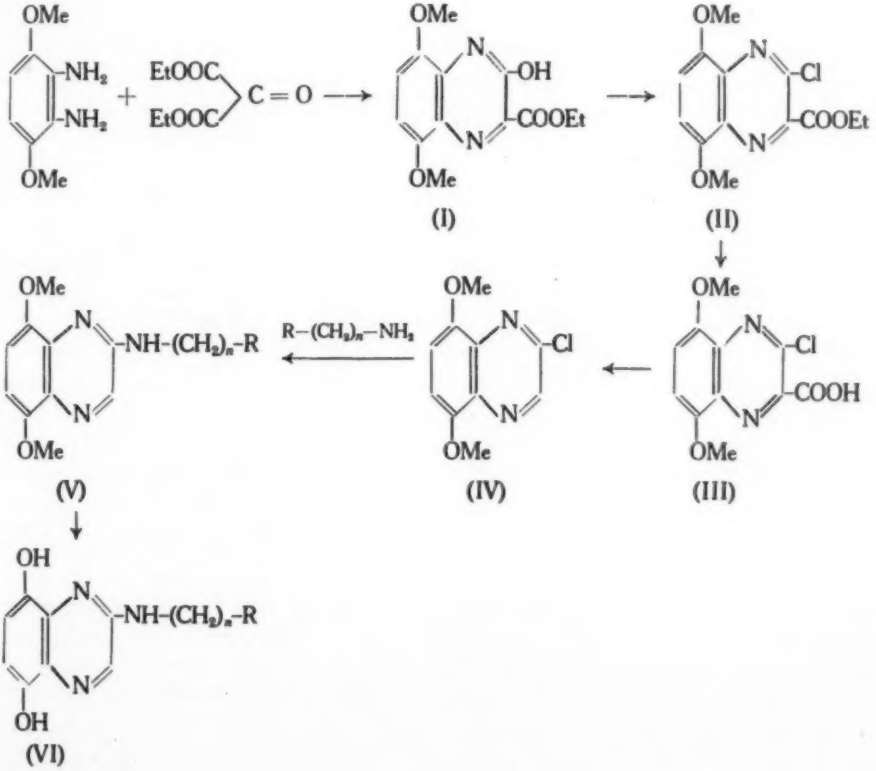
Several substituted dihydroxy- and dimethoxy-quinoxalines have been prepared for studying their antiamoebic activity.

The amoebacidal activity of oxine and its derivatives is attributed by some workers to chelation with traces of polyvalent metals like iron or cobalt to form feebly dissociated complexes, which are toxic in nature (Albert *et al.*, *Med. J. Austrl.*, 1944, **31,** 245; *Brit. J. Exp. Path.*, 1947, **28,** 69). Thompson *et al.* (*Amer. J. Trop. Med. Hyg.*, 1955, **4,** 224) and Burkhalter *et al.* (*J. Amer. Chem. Soc.*, 1954, **76,** 4902) from their studies of halogenated 8-hydroxyquinolines have conclusively proved that chelation only is responsible for the amoebacidal activity of these compounds and not the presence of halogen atoms in them. These observations led us to synthesise derivatives of dihydroxyquinoxaline, which have two chelating centres in the molecule and should therefore be more active than oxine, if chelation is mainly responsible for amoebacidal activity.

The steps involved in the synthesis of 3-substituted-5,8-dihydroxyquinoxalines are given below.



Starting from hydroquinone, 1,4-dimethoxy-2,3-diaminobenzene was prepared by a 3-step synthesis according to Lester *et al.* (*J. Org. Chem.*, 1959, **24,** 1451). It was then condensed with ethyl oxomalonate in ethanol to yield 3-hydroxy-2-ethoxycarbonyl-5,8-dimethoxyquinoxaline (I), which was then refluxed with $POCl_3$, wherby the -OH group in position 3 was replaced by a chlorine atom. The chloro compound, thus obtained, was hydrolysed by sodium carbonate in 75% ethanol to 3-chloro-5,8-dimethoxyquinoxaline-2-carboxylic acid. The acid was decarboxylated by heating it at its m.p. for 2 to 3 minutes to (IV). The 3-chloro-5,8-dimethoxyquinoxaline (IV) obtained was changed to 3-substituted-5,8-dimethoxyquinoxaline by the action of different amines in ethanol on (IV) in presence of calcined potassium carbonate. The dimethoxyquinoxalines were then hydrolysed with 48% hydrobromic acid to the corresponding dihydroxy derivatives.

EXPERIMENTAL

2,3-Diamino-1,4-dimethoxybenzene.—The starting material for this was 1,4-dimethoxybenzene, which was prepared from hydroquinone according to Dyson *et al.* (*J. Chem. Soc.*, 1927, 440). It was nitrated in glacial acetic acid with fuming nitric acid in the cold (Habermann, *Ber.*, 1878, **11,** 1035; Nietzki and Reckberg, *Ber.*, 1890, **23,** 1215). The required 2,3-dinitro-1,4-dimethoxybenzene was isolated by fractional crystallisation of the nitrated product from ethyl acetate. This was reduced catalytically to the diamino compound in ethanol using platinum oxide as catalyst, following the method of Lester *et al.* (*loc. cit.*), m.p. 84-85° (Lester *et al.* record m.p. 85-87°).

3-Hydroxy-2-ethoxycarbonyl-5,8-dimethoxyquinoxaline (I).—As difficulties were encountered in the isolation of the free diaminodimethoxybenzene, it was directly condensed after reduction of 2,3-dinitro-1,4-dimethoxybenzene as follows. The dinitro compound (4.56 g., 0.02 *M*) was dissolved in ethanol (100 c.c.) and catalytically reduced in presence of platinum oxide. The catalyst was removed by filtration and the filtrate was mixed with ethyl oxomalonate (3.48 g., 0.02 *M*) ("Org. Synthesis", Vol. I, p. 261), and the mixture refluxed on a water bath for 4 hours. Yellow-green shining crystals separated on cooling, which were filtered and washed with little ethanol, m.p. 242°. (Found : N, 9.57. $C_{13}H_{14}O_5N_2$ requires N, 10.07%).

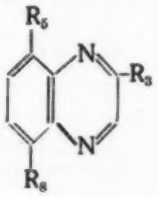
3-Chloro-2-ethoxycarbonyl-5,8-dimethoxyquinoxaline (II).—The compound (I, 5.5 g.) was heated with $POCl_3$(30 c.c.) at 120-30° in an oil bath for 1 hour. Excess of $POCl_3$ was removed under reduced pressure and the residue decomposed with ice. The chloro compound was then extracted with ether and finally recrystallised from ethanol, m.p. 154°, yield 5.4 g. (Found : N, 9.88. $C_{13}H_{13}O_4N_2Cl$ requires N, 9.44%).

3-Hydroxy-5,8-dimethoxyquinoxaline-2-carboxylic Acid (VII).—The quinoxaline (II, 1.2 g.) was heated with 10% NaOH solution for 15 minutes, cooled, and acidified with HCl (dil.) to Congo red (according to a method of Gowenlock, *J. Chem. Soc.*, 1945, 623). A red compound was obtained, which was purified by dissolving it in sodium bicarbonate solution and reprecipitating it with HCl (dil.), m.p. 213°, yield 0.9 g. (Found : N, 10.87. $C_{11}H_{10}O_5N_2$ requires N, 11.20%).

3-Chloro-5,8-dimethoxyquinoxaline-2-carboxylic acid (III) was prepared by hydrolysing a mixture of (II, 6.0 g.) with sodium carbonate (3.0 g.) in 200 c.c. of 75% ethanol on a water bath for 4 hours, following the method of Gowenlock (*loc. cit.*). Ethanol was removed and the residue was dissolved in water and acidified with HCl (dil.) to Congo red. An orange-coloured compound was obtained, which was further purified by dissolving it in sodium bicarbonate solution and reprecipitating it with HCl (dil.), m.p. 168°, yield 5.0. (Found : N, 9.96. $C_{11}H_9O_4N_2Cl$ requires N, 10.42%).

3-Chloro-5,8-dimethoxyquinoxaline (IV).—The above acid (III, 5.0 g.) was melted in a porcelain dish and the temperature was maintained for 2 to 3 minutes. After cooling it was extracted with sodium bicarbonate solution to remove the unchanged acid and filtered. The precipitate was recrystallised from ethanol, m.p. 128°, yield 3.4 g. (Found : N, 12.22. $C_{10}H_9O_2N_2Cl$ requires N, 12.47%).

TABLE I



	Substituted quinoxalines.				Picrolonates.		
R_3	M.P.	Yield.	%Nitrogen. Found.	Calc.	M.P.	%Nitrogen. Found.	Calc.
			R_5 & R_8 = dimethoxy.				
Diethylaminopropylamino-	152°	31%	17.33	17.61	210-12°	18.91	19.24
Piperidinopropylamino-	146°	48	16.59	16.96			
Morpholinopropylamino-	153°	42	16.58	16.86	265°	18.32	18.79
Benzylamino-	138-39°	61	13.98	14.23			
Ethanolamino-	148°	57	16.42	16.86	300°	18.46	19.10
Glycino-	144°	69	15.54	15.96			
			R_5 & R_8 = dihydroxy.				
Diethylaminopropylamino-	221°	69	18.82	19.31			
Piperidinopropylamino-	209-10°	83	18.11	18.54			
Morpholinopropylamino-	215°	92	18.07	18.42			
Benzylamino-	199°	94	15.26	15.73			
Ethanolamino-	196-97°	80	19.08	19.00			
Glycino-	151°	64	17.36	17.87			

3,5,8-Trihydroxyquinoxaline-2-carboxylic Acid (VIII).—The compound (I, 0.5 g.) was heated under reflux with 48% HBr (5 c.c.) for 15 minutes. It soon dissolved and then deposited red crystals after some times, which were filtered and washed with water. It dissolves in sodium bicarbonate solution with evolution of CO_2 showing thereby the presence of —COOH group formed by hydrolysis of the COOEt group of (I), m.p. 223°, yield 0.2 g. (Found : N, 12.19. $C_9H_6O_5N_2$ requires N, 12.61%). It was also obtained by hydrolysis of compound (VII) with HBr.

3-Chloro-5,8-dihydroxyquinoxaline-2-carboxylic acid (IX) was obtained by hydrolysis of both (II) and (III). Compound (II, 0.3 g.) was heated with 48% HBr (5 c.c.) till a red compound separated out (about ½ hour), which was then isolated in the usual way, m.p. 228°, yield 0.2 g. (Found : N, 11.50. $C_9H_5O_4N_2Cl$ requires N, 11.64%).

3-Chloro-5,8-dihydroxyquinoxaline (X) was obtained by hydrolysis of (IV, 0.56 g.) with 48% HBr (5 c.c.) for 1 hour. After cooling, the mixture was neutralised with sodium carbonate solution and concentrated on a water bath almost to dryness. The residue was extracted with dry chloroform, the solvent removed, and the residue recrystallised from 95% ethanol, m.p. 211°, yield 0.4 g. (Found : N, 14.61. $C_8H_5O_2N_2Cl$ requires N, 14.24%).

Dialkylaminoalkylamines were prepared by reduction of the corresponding dialkylaminoalkyl nitriles, following the method of Holcomb and Hamilton (*J. Amer. Chem. Soc.*, 1942, **64**, 1309).

3-Substituted-5,8-dimethoxyquinoxalines.—A mixture of 3-chloro-5,8-dimethoxyquinoxaline (0.005 *M*), the appropriate amino compound (0.005 *M*) in 50 c.c. ethanol, and calcined potassium carbonate (0.0025 *M*) was refluxed for 4 to 8 hours. Completion of the reaction was confirmed by a change of colour of the reaction mixture. Potassium chloride formed was filtered off, solvent removed, and the residue obtained was recrystallised from a suitable solvent. A few of the quinoxalines were characterised through their picrolonates (Table I).

3-Substituted-5,8-dihydroxyquinoxalines were prepared from 3-substituted 5,8-dimethoxyquinoxaline (0.002 *M*) by hydrolysing with 48% HBr (5 c.c.) for 1 hour. After cooling it was neutralised with sodium carbonate solution. The solution was evaporated to dryness on a water bath and the dihydroxy compound extracted with chloroform. The chloroform extract was dried. The product obtained after removal of the solvent was recrystallised from ethanol.

The m.p., yields and analytical data of 3-substituted-5,8-dimethoxy- and -5,8-dihydroxyquinoxalines are reported in Table I.

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Studies on the Citrate Complex of Calcium

Rabindra K. Patnaik and S. Pani

The citrate complex of calcium has been investigated by the *p*H titration method in the *p*H range of 7.1 to 7.25. The equilibrium constant of the reaction,

$$Ca^{2+} + Cit^{3-} \rightleftharpoons CaCit^{-}$$

is 2.66×10^3.

Hastings and collaborators (*J. Biol. Chem.*, 1934, **107**, 351) determined the stability constant of the calcium citrate chelate by the biological assay method and found the equilibrium constant to be 1.585×10^3. They could not detect the existence of complexes with more than one ligand.

From conductance and transport measurements Henning *et al.* (*Z. Kinderh.*, 1951, **69**, 55) observed reaction between Ca^{2+} and citrate ion to form $CaCit^{-}$, independent of *p*H.

Schubert and Lindenbaum (*J. Amer. Chem. Soc.*, 1952, **74**, 3529) studied the complex formation between Ca^{2+} and a series of organic acids. These complexes are of 1 : 1 type. The formation constant of calcium citrate complex is found to be 1.445×10^3.

EXPERIMENTAL

A very pure sample of calcium carbonate was added in excess to *M*/5 perchloric acid solution (125 c.c.) so that some solid was left undissolved. The solution was boiled to remove CO_2 present, cooled, and left for about 4 hours. It was then filtered to a 250 c.c. measuring flask and diluted to the mark. The solution was estimated for calcium content by oxalate method and found to contain *M*/20 calcium perchlorate.

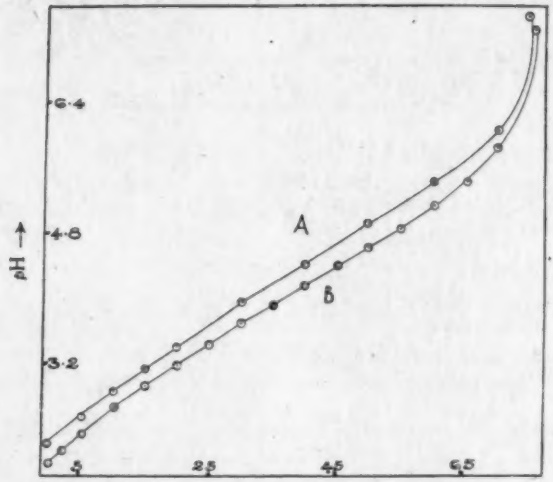
Experiment I.—Curve A (Fig. 1) represents the results obtained by titrating 200 c.c. of a solution containing 0.025 g. mole of citric acid and curve B represents the results obtained by titrating 0.025 g. mole of citric acid and 0.0025 g. mole of calcium perchlorate against *N*-NaOH at 33°.

Experiment II.—Curve A (Fig. 2) represents the results obtained by titrating 100 c.c. of a solution containing 0.025 g. mole of sodium perchlorate and curve B represents that of another solution containing 0.025 g. mole of sodium perchlorate and 0.00125 g. mole of calcium perchlorate against 0.1 *M* sodium citrate at 33°.

DISCUSSION

In experiment (I) the *p*H of the system B is little lower than that of the system A. The horizontal distance between the two curves increases in the beginning, then decreases, and finally becomes negligible after *p*H 6.0. The small horizontal distance between the two curves, especially the negligible distance at the neutralisation point of the citric acid, indicates that no acid is liberated. The low *p*H in the system B may be ascribed to removal of citrate ligand from the solution by calcium ions due to complex formation.

FIG. 1

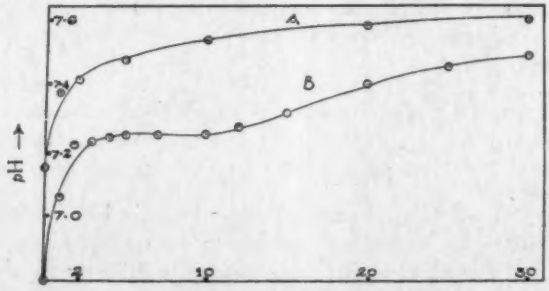


Amount of N sodium hydroxide added in c.c.

In experiment (II) the *p*H of the system (B), which contains calcium, is lower than that of the other system. This is probably due to the removal of citrate ion from the solution by the calcium ion on account of formation of the complex. The added citrate ion is most probably removed partially from the solution and hence the *p*H of the system does not rise as rapidly as found in curve A.

The *p*H of the solution rises only after the addition of very nearly one g. mole of sodium citrate per g. mole of calcium perchlorate. This indicates the formation of a very stable 1 : 1 complex.

FIG. 2



Amount of 0.1M sodium citrate added in c.c.

Calculation of the Equilibrium Constant

Due to the reaction of citrate ion and Ca^{2+}, no acid is liberated. Hence the complex would be $CaCit^-$. In experiment (II) the reaction may be represented by equation (1) and the equilibrium constant by equation (1-1).

$$Ca^{2+} + Cit^{3-} \rightleftharpoons CaCit^- \quad .. \quad (1)$$

$$\frac{[CaCit^-]}{[Ca^{2+}]\,[Cit^{3-}]} = K \quad .. \quad (1\text{-}1)$$

where $[CaCit^-]$, $[Ca^{2+}]$, and $[Cit^{3-}]$ represent the molar concentration of $CaCit^-$ complex, calcium ion, and free citrate ion respectively.

Let A and B be the two points on the same *p*H axis on curves A and B respectively. Let $[Ct]_A$, $[Cit^{3-}]_A$, $[Ct]_B$, $[Cit^{3-}]_B$, and $[Ca(ClO_4)_2]$ represent the molar concentration of total citrate at A, free citrate at A, total citrate at B, and free citrate ion at B, and calcium perchlorate respectively.

It is assumed that Ca^{2+} is not hydrolysed at *p*H 7.1 to 7.3. Hence the *p*H of the solution depends on the concentration of citrate ion.

It is further assumed that at the same *p*H, the citrate ion concentration in the systems A and B is the same. Hence the free citrate ion concentration at A and B is equal to $[Cit^{3-}]_A$.

$$\text{Total citrate at A} = [Ct]_A = [Cit^{3-}]_A \quad .. \quad (2)$$

$$\text{Total citrate at B} = [Ct]_B = [Cit^{3-}]_A + [CaCit^-] \quad .. \quad (2\text{-}1)$$

$$\text{Hence } [CaCit^{3-}] = [Ct]_B - [Ct]_A \quad .. \quad (2\text{-}2)$$

$[Ca(ClO_4)_2]$ is calculated from the g.moles of calcium perchlorate taken and the total volume of the solution $[Ct]_A$ and $[Ct]_B$ is calculated from g.moles of sodium citrate added and volume of the solution at A and B respectively.

$[Ca^{2+}]$ can be calculated by subtracting $[CaCit^-]$ from $[Ca(ClO_4)_2]$.

TABLE I

*p*H.	$[Cit^{3-}] \times 10^4$.	$[Ct]_B \times 10^3$.	$[Ca(ClO_4)_2] \times 10^3$.	$[CaCit^-] \times 10^3$.	$[Ca^{2+}] \times 10^3$.	$K \times 10^{-3}$.
7.17	0.9988	1.380	1.233	1.281	11.05	1.160
7.22	2.990	2.334	1.221	2.045	10.17	0.723
7.23	3.985	3.482	1.209	3.084	9.01	0.8592
7.24	3.985	3.661	1.204	3.263	8.78	0.9326
7.24	3.985	3.847	1.201	3.449	8.56	1.011
7.25	3.985	5.661	1.180	5.263	6.54	2.018
7.25	3.985	5.927	1.176	5.529	6.23	2.227
7.25	3.985	6.542	1.168	6.144	5.54	2.784
7.25	3.985	7.408	1.157	7.010	4.56	3.858
7.25	3.985	8.256	1.147	7.858	3.61	5.463

The equilibrium constant K is calculated at different *p*H values by equation (1-1). The values are tabulated in Table I. The mean value of K is found to be 2.66×10^3. This is in good

agreement with the value obtained by Schubert and Hindenbaum (*loc. cit.*) and also with that obtained by Hastings *et al.* (*loc. cit.*).

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Studies on the Citrate Complex of Beryllium

Rabindra K. Patnaik and S. Pani

The citrate complex of beryllium has been studied in the *p*H range of 2.6 to 6.0. Beryllium ions react with citric acid and form in the lower *p*H region a neutral complex (C) liberating two protons according to the reaction :

$$Be^{2+} + H_3Cit \rightleftharpoons C + 2H^+ \quad .. \quad .. \quad .. \quad (i)$$

In the higher *p*H range this neutral complex dissociates like a dibasic acid to complexes C_1^- and C_2^{2-} according to reactions (*ii*) and (*iii*) :

$$C \rightleftharpoons C_1^- + H^+ \quad .. \quad .. \quad .. \quad (ii)$$

$$C_1^- \rightleftharpoons C_2^{2-} + H^+ \quad .. \quad .. \quad .. \quad (iii)$$

The equilibrium constants of reactions (*i*), (*ii*), and (*iii*) are found to be 4.52×10^{-4}, 2.41×10^{-4}, and 4.95×10^{-6} respectively.

From dialysis studies of Be-Cit system in bicarbonate buffer, Feldman and co-workers (*J. Amer. Chem. Soc.*, 1951, **73,** 4775) found Be^{2+} and citrate ions to combine to form a stable complex at *p*H 8.25 in maximum molar ratio of 2.

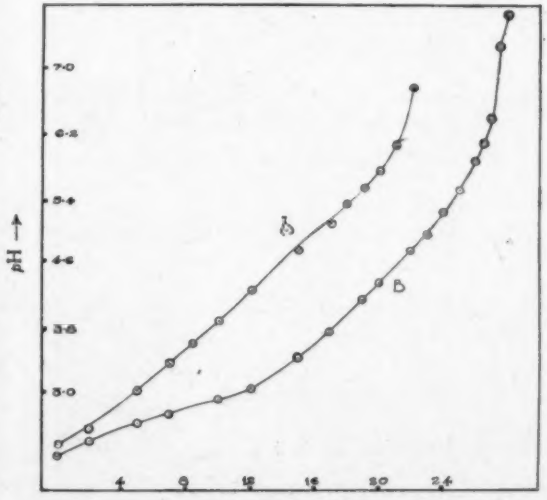
Feldman *et al.* (*ibid.*, 1955, **77,** 878) also studied the same system by ion-exchange method and observed that Be^{2+} did not form any complexes with H_3Cit, but did so with H_2Cit^-, $HCit^{2-}$, and Cit^{3-}. The instability constants (*K*) of BeH_2Cit^+, BeHCit, and $BeCit^-$ are 4×10^{-2}, 6×10^{-3}, and 3×10^{-5} respectively.

From the results obtained above *p*H 4.0, they have inferred the presence of polynuclear complexes, such as, $Be_2(HCit)_2$. A complex having a charge more negative than -1 is present above *p*H 7.0.

EXPERIMENTAL

A very pure sample of beryllium carbonate was dissolved in a known excess of perchloric acid to prevent hydrolysis. The solution was boiled to remove carbon dioxide and then made to 500 c.c. The beryllium content was determined by precipitating as hydroxide and then igniting to BeO_2.

FIG. 1

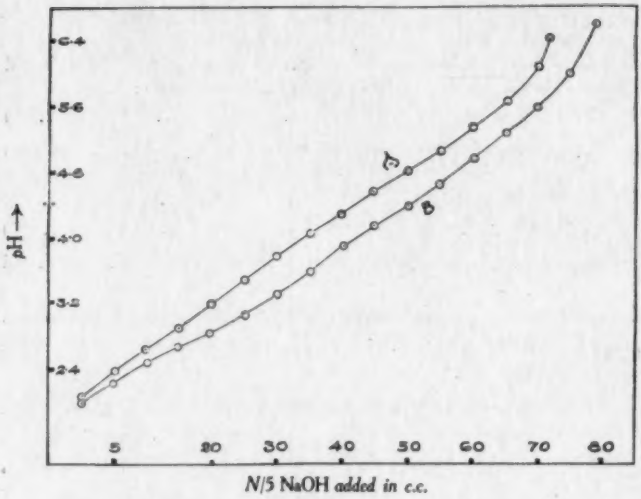


Experiment I.—Curve A (Fig. 1) represents the results obtained by titrating 100 c.c. of the solution containing 0.0015 g. mole of citric acid and 0.025 g. mole of soidum perchlorate against *N*/5-NaOH at 32°.

Curve B represents the results obtained by titrating the same volume of another solution containing 0.001059 g. mole of beryllium perchlorate (in presence of known excess of perchloric acid which was neutralised by standard alkali before diluting to 100 c.c.), 0.0015 g.mole of citric acid, and 0.025 g.mole of sodium perchlorate against *N*/5-NaOH at 32°.

Expriment II.—Curve A (Fig. 2) represents results obtained by titrating 100 c.c. of the solution containing 0.005g. mole of citric acid and 0.025 g. mole of sodium perchlorate against *N*/5-NaOH at 32°.

FIG. 2



Curve B represents the results obtained by titrating 100 c.c. of another solution containing 0.005 g.mole of citric acid and 0.001059 g.mole of beryllium perchlorate (in presence of known excess of perchloric acid, which was neutralised by standard alkali before diluting to 100 c.c.) and 0.025 g. mole of sodium perchlorate against *N*/5-NaOH.

Experiment III.—Curve A (Fig. 3) represents the results obtained by titrating 150 c.c. of a solution containing 0.020 g.mole of sodium citrate and 0.032 g.mole of sodium perchlorate against 0.1*N*-NaOH at 32°.

Curve B represents the results obtained by titrating 150 c.c. of another solution containing 0.001059 g.mole of beryllium perchlorate (in presence of known excess of perchloric acid, which was neutralised by standard alkali before diluting to 100 c.c.), 0.020 g.mole of sodium citrate, and 0.032 g.mole of sodium perchlorate against 0.1*N*-NaOH at 32°.

DISCUSSION

The *p*H of the system (B) in each case is lower than the corresponding *p*H in the system (A), indicating the liberation of acid. The horizontal distance between the two curves increases in the beginning and then decreases. The two curves, however, diverge again above *p*H 6.

In experiment (II), where the metal to ligand ratio is 1 : 5, the horizontal distance is very nearly constant. This indicates the formation of a complex with a constant metal to ligand ratio throughout the *p*H range.

The concentration of the ligand compared to the metal being large, the horizontal distance between the two curves is roughly the measure of the amount of acid liberated. It is therefore found from experiment (II) that one equivalent of acid per atom of Be is liberated. It is therefore very probable that the complex formed contains one ligand per atom of Be.

Calculation of the Equilibrium Constant

The reactions taking place in experiments (I) and (II) are assumed to be similar to that in the citrate complexes of cadmium (Patnaik and Pani, this *Journal*, 1957, **34**, 673) and may be

represented by equation (I) and the equilibrium constant by equation (I-1).

$$Be^{2+} + H_3Cit \rightleftharpoons C + nH^+ \quad .. \quad .. \quad (I)$$

$$\frac{[C]\,[H^+]^n}{[Be^{2+}]\,[H_3Cit]} = K \quad .. \quad .. \quad (I\text{-}1)$$

By proceeding in a similar manner (Patnaik and Pani, *loc. cit.*) it can be shown that

$$\frac{\Delta[NaOH] - \frac{a}{b}\Delta[Ct]}{[C]} = n - \frac{a}{b}$$

and when the formation of the complex is complete

$$\frac{\Delta[NaOH] - \frac{a}{b}\Delta[Ct]}{[Be(ClO_4)_2]} = n - \frac{a}{b}$$

Δ [NaOH], $-\Delta$ [Ct], [$Be(ClO_4)_2$], a, and b are calculated as before.

Substituting these values, a series of values of n calculated has been collected in Table I.

TABLE I

pH.	Δ [NaOH] $\times 10^3$.	$-\Delta$[Ct] $\times 10^4$.	[$Be(ClO_4)_2$] $\times 10^3$.	a/b.	n.	[C]$\times 10^3$.	[Be^{2+}]$\times 10^3$.	[H_3Cit] $\times 10^3$.	$K\times 10^4$.
2.6	5.58	4.2	10.07	0.2560	0.8210	3.261	6.810	8.233	3.670
2.7	6.39	4.8	9.961	0.3046	0.9607	3.856	6.105	7.201	3.491
2.8	8.05	7.1	9.804	0.3588	1.2055	5.085	4.746	5.741	4.663
2.9	9.43	7.1	9.642	0.4184	1.4274	6.148	3.494	4.471	6.237
3.5	12.38	9.3	9.168	0.8351	2.2691				
3.6	12.40	9.4	9.118	0.9078	2.3608				
3.7	12.12	9.0	9.072	0.9797	2.4127				
3.8	11.84	9.0	9.040	1.052	2.466				
3.9	11.72	8.7	8.974	1.127	2.543				
4.0	12.06	9.0	8.935	1.204	2.675				
4.1	11.67	8.7	8.913	1.282	2.716				
4.2	11.57	8.7	8.876	1.362	2.799				
4.3	11.31	8.5	8.839	1.445	2.863				
4.8	10.26	7.7	8.664	1.876	3.227				
5.0	9.65	7.2	8.602	2.049	3.342				
5.2	8.94	6.6	8.545	2.213	3.430				
5.5	8.21	6.2	8.470	2.450	3.599				
5.8	7.53	5.7	8.410	2.653	3.728				
6.0	7.33	5.5	8.375	2.754	3.860				

The values of n gradually increases with pH, but less than 2 in the region below pH 3.2, less than 3 in the region below pH 4.4, and more than 3 but less than 4 above pH 4.5. Below pH 3.2, the complex is formed with the liberation of two protons due to the reaction of beryllium ion and citric acid. Hence the complex is a neutral one. This subsequently dissociates like a dibasic acid in two steps. The reactions are given by equations (2) and (3) and the equilibrium constants are represented by equations (2-1) and (3-1).

$$C \rightleftharpoons C_1^- + H^+ \quad .. \quad .. \quad (2)$$

$$\frac{[C_1^-]\,[H^+]}{[C]} = K_1 \quad .. \quad .. \quad (2\text{-}1)$$

$$C_1^- \rightleftharpoons C_2^{2-} + H^+ \quad .. \quad .. \quad (3)$$

$$\frac{[C_2^{2-}]\,[H^+]}{[C_1^-]} = K_2 \quad .. \quad .. \quad (3\text{-}i)$$

K, K_1, and K_2 are calculated, as determined before, and tabulated in Tables I—III respectively. The mean values of K, K_1, and K_2 are 4.520×10^{-4}, 2.410×10^{-4}, and 4.95×10^{-6} respectively.

TABLE II

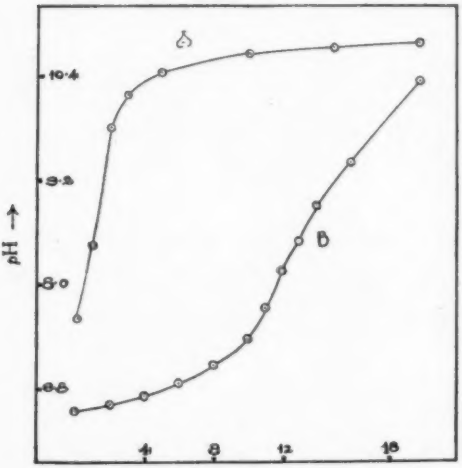
pH.	*n*-2.	3-*n*.	$K_1 \times 10^4$.	pH.	*n*-2.	3-*n*.	$K_1 \times 10^4$.
3.5	0.2691	0.7309	1.165	4.0	0.675	0.3250	2.077
3.6	0.3608	0.6392	1.418	4.1	0.716	0.2840	2.003
3.7	0.4127	0.5873	1.403	4.2	0.799	0.2010	2.508
3.8	0.4660	0.5340	1.383	4.3	0.863	0.1370	3.157
3.9	0.5430	0.4570	1.496				

TABLE III

pH.	*n*-3.	4-*n*.	$K_2 \times 10^6$.	pH.	*n*-3.	4-*n*.	$K_2 \times 10^6$.
4.8	0.227	0.773	4.654	5.5	0.599	0.401	4.724
5.0	0.342	0.658	5.198	5.8	0.728	0.272	4.241
5.2	0.430	0.570	4.760	6.0	0.860	0.140	6.124

In experiment (III) (Fig. 3) the curves are similar to those obtained in the case of cadmium citrate and other systems. Here also the curve B is similar to the neutralisation curve of a strong acid. The pH of the system (B), attained by the addition of 12 c.c. of 0.1 *N*-NaOH, is reached by the system (A) on the addition of only 1 c.c. of NaOH. Hence 11 c.c. of 0.1*N*-NaOH is consumed by the complex formed from 0.001059 g.mole of beryllium perchlorate.

FIG. 3



O. O*N*-NaOH *added in c.c.*

The liberation of one proton indicates the presence of a beryllium citrate complex having two negative charges (C_2^{2-}).

The structure of the beryllium citrate complexes are just similar to those of the nickel and cadmium citrate already discussed (Patnaik and Pani, this *Journal*, 1957, **34**, 619).

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Complex Compounds of Nickel and Copper with 2-Guanidinobenzimidazole*

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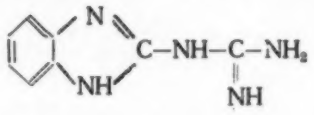
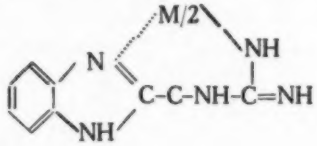
Several complex compounds of nickel and copper with 2-guanidinobenzimidazole have been prepared and their properties studied. Halides, nitrates and sulphates of the complex base, and also the complex hydroxides have been prepared. The complex nickel hydroxide has been obtained in three differently coloured modifications whereas the chloride and sulphate have been obtained in two different colours. All nickel complexes are diamagnetic and hence planar with dsp^2 bonding. The copper complexes do not show any colour change; these are either green or bluish green and paramagnetic (μ-1.76 to 1.83 B.M.).

Ziegelbauer (*Chem. Zentrl.*, 1897, I, 9) first obtained a base, $C_8H_9N_5$, by refluxing a mixture of dicyandiamide and *o*-phenylenediamine hydrochloride in ethanol and termed it *o*-phenylenebiguanide.

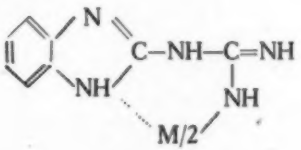
Pellizzari (*ibid.*, 1921, **III,** 527) obtained the same base by refluxing a mixture of *o*-phenylenediamine hydrochloride and dicyandiamide in water and represented it as :



Dubsky, Langer and Strand (*Coll. Czech. Chem. Comm.*, 1938, **10,** 103) reported the preparation of two complex compounds of copper and nickel with *o*-phenylenebiguanide having the composition : $(C_8H_8N_5)_2Cu.H_2SO_4.2H_2O$ and $(C_8H_8N_5)_2$ $Ni.H_2SO_4.4H_2O$, represented by (I) or (II).



(I)

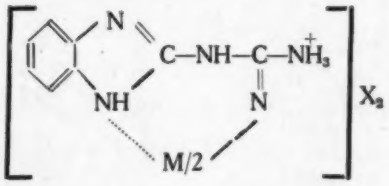


(II)

Though the base, $C_8H_9N_5$, resembles biguanide in its reactions with metal ions, it is actually an iminazole derivative and has been wrongly termed as *o*-phenylenebiguanide by the above workers. It has therefore been named 2-guanidinobenzimidazole.

* The "so called" *o*-phenylenebiguanide of Ziegelbauer.

In view of the constitution of metal biguanide complexes advaned by Rây and Saha (this *Journal*, 1937, **14,** 670), the above structure for the nickel and copper complexes of 2-guanidinobenzimidazole cannot be justified and it should be represented as :



(where M is a bivalent metal like Cu, Ni, and Co and X is a monovalent anion or its equivalent acid radical).

The nickel complexes have been obtained in differently coloured modifications, viz., brick-red, light pink, and violet. Rây and Chakravarty (*ibid.*, 1941, **18,** 609) have obtained with phenylbiguanide, nickel complexes with two different colour modifications. With the present knowledge of these substances it is not possible to assume a cause for the occurrence of such colour modifications. Copper complexes showed no such behaviour. This was also the case with phenylmethylbiguanide (Ghosh and Chatterjee, *ibid.*, 1953, **30,** 369) and with *p*-phenetylbiguanide (Ghosh and Banerjee, *ibid.*, 1955, **32,** 32). Complexes of copper with biguanide or substituted biguanide are usually rose-red or pink in colour; 2-guanidinobenzimidazole (the so-called *o*-phenylenebiguanide) complexes of copper are, however, green or bluish green and less stable than the biguanide complexes as is evident from the fact that the latter can easily displace 2-guanidinobenzimidazole in its copper complexes. A green variety of copper-phenylbiguanide *p*-sulphonic acid was reported by Rây and Dutt (*ibid.*, 1948, **25,** 569) with a magnetic moment value of 1.84 B.M.

The nickel complexes are diamagnetic and are square planar with $3d4s4p^2$ bonding. The copper complexes are paramagnetic; their magnetic moments lie between 1.76 and 1.83 B.M. According to Rây and Sen (*ibid.*, 1948, **25,** 473), the bonding in the copper complexes should be $4s4p4d^2$. This view is also supported by Craig *et al.* (*J. Chem. Soc.*, 1954, 349).

EXPERIMENTAL

2-Guanidinobenzimidazole was prepared by refulxing a mixture of *o*-phenylenediamine hydrochloride (1 *M*) and dicyandiamide (2 *M*) in water for 5 to 6 hours. The precipitated compound was filtered, dissolved in HCl (dil.), and reprecipitated by NaOH. The compound was obtained in plates, m.p. 246-47° (Pelliazari, *loc. cit.*, reports m.p. 245°). (Found : C, 53.69; H,5.19. $C_8H_9N_5$ requires C, 54.85; H, 5,14%).

Nickel Complexes

α-Nickel-2-guanidinium Benzimidazole Hydroxide.—A dilute solution of NaOH was added dropwise to a solution of nickel chloride (1 *M*) and 2-guanidinobenzimidazole in HCl (dil.) (2 *M*), when a light pink precipitate separated, which gradually changed to dirty brick-red on standing. The precipitate was rapidly filtered, washed with cold water and ethanol, and dried over NaOH. {Found : Ni, 11.80; N, 28.10. $[Ni(C_8H_9N_5)_2](OH)_2,3H_2O$ requires Ni, 11.82; N, 28.18%}. It is the most stable of the three varieties. It slowly dissolves in hot water forming a light green solution.

β-Nickel-2-guanidinium Benzimidazole Hydroxide. — When a dilute solution of ammonium hydroxide was substituted for NaOH solution in the above preparation, a light pink variety of the complex base separated. It was washed and dried as before. {Found : Ni, 12.26 ; N, 29.36. $[Ni(C_8H_9N_4)_2](OH)_2$, $2H_2O$ requires Ni, 12.31 ; N, 29.37%}.

This variety slowly changes into the α-variety when kept suspended in water or heated over a water bath.

γ-Nickel-2-guanidinium Benzimidazole Hydroxide.—The light pink base, initially obtained in the preparation of the α-complex, was dissolved in HCl (dil.). A little ammonium hydroxide solution was then added, followed by NaOH, when a violet solution was obtained from which a violet precipitate separated on standing. It was washed and dried as above. On drying the colour changed to dirty violet. {Found : Ni, 11.78 ; N, 28.12. $[Ni(C_8H_9N_5)_2](OH)_2$, $3H_2O$ requires Ni, 11.82 ; N, 28.18%}.

This does not change to the α variety on heating over a water bath. All the different bases liberate ammonia from ammonium salts and are insoluble in hot water.

α-Nickel-2-guanidinium Benzimidazole Chloride.—The complex α-base was suspended in water and was treated with an excess of ammonium chloride on a water bath till the evolution of ammonia had ceased. The yellowish pink precipitate was thoroughly washed with ice-cold water and ethanol and dired in air. {Found : Ni, 11.38 ; Cl, 13.80 ; N, 27.20. $[Ni(C_8H_9N_5)_2]Cl_2$, $2H_2O$ requires Ni, 11.39 ; Cl, 13.76 ; N, 27.14%}.

The chloride is slightly soluble in cold water forming a light green solution. Other complex salts were similarly prepared by metathesis of the complex base with the respective ammonium salt.

β-Nickel-2-guanidinium benzimidazole chloride is orange in colour. (Found : Ni, 11.32. Calc. Ni, 11.39%).

The orange-coloured β-chloride, when suspended in water and heated on a water bath, changed to the yellowish pink α-variety.

α-Nickel-2-guanidinium Benzimidazole Bromide and Iodide.—The bromide was obtained in yellowish pink colour. {Found : Ni, 9.18 ; Br, 25.10. $[Ni(C_8H_9N_5)_2]Br_2.4H_2O$ requires Ni, 9.16 ; Br, 24.97%}. The β- and γ-bases on similar treatment gave the same yellowish pink α-bromide. The iodide is pink in colour. {Found : Ni, 8.40 ; I, 36.48. $[Ni(C_8H_9N_5)_2]I_2$, $2H_2O$ requires Ni, 8.41 ; I, 36.35%}.

α-Nickel-2-guanidinium Benzimidazole Sulphates.— The complex α-sulphate was obtained by metathesis of the base with ammonium sulphate in brick-red colour. {Found : Ni, 10.48 ; SO_4, 17.54. $[Ni(C_8H_9N_5)_2]SO_4.3H_2O$ requires Ni, 10.50 ; SO_4, 17.18%}. From the β-base the sulphate was obtained in yellowish buff colour. {Found: Ni, 10.22; SO_4, 16.70. $[Ni\ (C_8H_9N_5)_2]\ SO_4$, $4H_2O$ requires Ni, 10.17 ; SO_4, 16.64%}.

The β-sulphate, when suspended in water and heated on a water bath, changed to the brick-red α-variety. The γ-base, however, on similar treatment yielded the brick-red coloured α-sulphate.

α-Nickel-2-guanidinium benzimidazole nitrate was obtained in dirty red colour. {Found : Ni, 10.69 ; Ni, 30.59. $[Ni(C_8H_9N_5)_2](NO_3)_2.H_2O$ requires Ni, 10.66 ; N, 30.50%}.

Copper Complexes

Copper-2-guanidinium Bnzimidazole Hydroxide.—To a solution of copper sulphate (1 *M*) and 2-guanidinobenzimidazole (2 *M*) in HCl (dil.) a dilute solution of NaOH was added dropwise

avoiding excess, when an olive-green precipitate was formed. The green precipitate was quickly filtered, washed with cold water, and dried over NaOH. {Found : Cu, 12.63 ; N, 27.98. $[Cu(C_9H_9N_5)_2]$ $(OH)_2,3H_2O$ requires Cu, 12.72 : N, 28.06%}.

The base is moderately soluble in hot water. It liberates ammonia from ammonium salts ; when neutralised with dilute mineral acids, corresponding complex salts are produced.

The salts of the complex copper-2-guanidinium benzimidazole base were obtained by the action of the corresponding ammonium salt on the base. The salts are paramagnetic. Colour and analyses of the complex salts are shown in Table I.

TABLE I

Complex salts of Cu.	Colour.	Formula.	%Copper. Found.	%Copper. Calc.	%Anion.	%Anion. Found.	%Anion. Calc.	μ (B.M.)
Chloride	Deep green	X. $Cl_2,7H_2O$	10.50	10.40	Cl :	11.60	11.62	1.82
Bromide	Dark „	X. $Br_2,2.5H_2O$	10.30	10.31	Br :	26.07	25.93	1.82
Iodide	„ „	X. $I_2,2H_2O$	9.01	9.01	I :	36.17	36.13	1.83
Nitrate	Bluish „	X. $(NO_3)_2,4H_2O$	10.43	10.41	N :	26.75	27.56	1.79
Sulphate	„ „	X. $SO_4,3H_2O$	11.21	11.27	SO_4 :	17.04	17.05	1.76

* X = $[Cu(C_9H_9N_5)_2]$

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Spectrophotometric Identification and Determination of *p*-Phenylenediamine Type of Antioxidants in Vulcanised Rubber **

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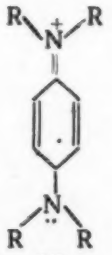
A method has been proposed for the identification and quantitative determination of antioxidants, derived from *p*-phenylenediamine. It consists in the formation of a highly coloured solution, presumably Wurster's salt, by a reaction of the diamine derivative with acidic permanganate in ethanolic media, and measurement of the absorption with a spectrophotometer. The method has been found suitable for all the four antioxidants studied and also for the *p*-phenylenediamine derivative present as one of the components in a mixed antioxidant.

Derivatives of *p*-phenylenediamine comprise an important class of antioxidants and antiozonants, used in the rubber industry. Several methods are reported in the literature (Burchfield and Judy, *Anal. Chem.*, 1947, **19,** 786; Endo, *J. Soc. Chem. Ind., Japan*, 1935, **38,** Suppl. binding, 618; Craig, *Ind. Eng. Chem., Anal. Ed.*, 1937, **9,** 56; Zijp, *Rec. trav. chim.*, 1957, **76,** 313, 317) for identification of these antioxidants along with other amine type of antioxidants. None of these methods, however, is satisfactory for estimation of these antioxidants. Recently, Hilton (*Rubber Age*, 1958, **84,** 263; *Anal. Chem.*, 1960, **32,** 383) reported a spectrophotometric method for identification and determination of a large number of antioxidants. The method consists in extracting the antioxidant from the rubber sample and formation of an azo dye by addition of a suitable coupling agent. This method was found satisfactory for many antioxidants, but for most of the derivatives of *p*-phenylenediamine, it was otherwise. No method, reported suitable for the determination of this type of antioxidants, has so far been evolved.

The derivatives of *p*-phenylenediamine are known to be oxidised very easily and in ethanolic alkaline solution these form strongly coloured quinone di-imines (Schneider, *Rubber Chem. Technol.*, 1957, **30,** 681), whereas in acidic solution Wurster's salts are believed to be formed. Michaelise *et al.* (*J. Amer. Chem. Soc.*, 1939, **61,** 1981) have examined the essential relationships between structure and stability in the highly coloured oxidation products of *p*-phenylenediamine and its alkyl derivatives; they have pointed out that stable radicals can only be formed when the Wurster's salts have a molecular symmetry sufficiently high for the occurrence of resonance throughout the whole molecule. For this, the benzene ring, the *para* nitrogen atoms, and the four attached groups must lie in one plane, since the contribution of the quinonoid canonical state (II) restricts the rotation of the amino groups.

(I)



(II)

Substitution of the amino groups of *p*-phenylenediamine enhances the stability of Wurster's salts, but substitution in the benzene ring tends to reduce their stability. The *p*-phenylenediamine

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** When this paper was being communicated, a similar work reported by C.L. Hilton (*Anal. Chem.*, 1960, **32,** 1554) was noticed which made use of the same principle but differed in experimental details.

type of antioxidants, used in the rubber industry and investigated by the present authors, satisfy these stability requirements, since all the substituents are on the amino-nitrogen and none on the benzene ring. The present method involves the formation of a highly coloured solution (possibly Wurster's salt) from the antioxidant in question by reaction with an oxidising agent, like potassium permanganate or potassium dichromate in acidified ethanol, and measurement of the absorbance with a spectrophotometer.

EXPERIMENTAL

The rubber mix used to ascertain the suitability of the method for the determination of the antioxidants in vulcanised rubber and also for studying the interference, if any, from the common rubber ingredients had the following composition by weight : Raw rubber (smoked sheet) = 100.0 ; ZnO = 5.0 ; stearic acid = 1.5 ; paraffin wax = 2.0 ; carbon black (SRF) = 20.0 ; whiting = 10.0 ; talcum powder = 10.0; Dutrex R = 1.0; MBTS=0.5; MBT = 0.5; ZDC = 0.1 ; sulphur = 3.0; antioxidant= 1 to 1.5. The mix was cured at 150° for 30 minutes.

Trade names of the four antioxidants used in the present investigation together with their chemical names and the corresponding wave lengths at maximum absorption are shown in Table I.

TABLE I

Trade name.	Chemical name.	λ_{max} (Fig. 1).
Antioxidant 4010	*N*-Phenyl-*N'*-cyclohexyl-P	600 mμ
Nonox DPPD	*NN'*-Diphenyl-P	380
UOP 88	*NN'*-Dioctyl-P	560
UOP 288	*NN'*-Dioctyl-P	560

P-denotes *p*-phenylenediamine.

The instrument used was a Hilger Unispek spectrophotometer with a temperature-regulated cell holder and quartz cells having a light path of 1.000 ±0.005 cm.

Ethanol, 95% glacial acetic acid (reagent grade), and potassium permanganate solution in water ($2.5 \times 10^{-3}M$) were used as reagents.

Procedure.—The absorptivities of the coloured solutions obtained according to the detailed procedure given below were measured at three different states of the antioxidants : (*a*), (*b*), (*c*) (*vide infra*).

(*a*). *Original Antioxidants in Ethanolic Solution.*—The antioxidant (0.5 g.) was dissolved in ethanol and made to 100 c.c. To the solution (1 c.c.) were added glacial acetic acid (2.5 c.c.) and aqueous $KMnO_4$ (1 c.c., $2.5 \times 10^{-3}M$) (*proportionately smaller amount for lower dilutions*). The colour developed immediately. The volume was made to 25 c.c. with 95% ethanol. The colour remained stable for at least 2 hours. Absorbance was measured soon after dilution taking ethanol containing the same concentration of the reagents in the reference cell of the spectrophotometer.

(*b*) & (*c*). *The Antioxidants Extracted from the Uncured and Cured Rubber.*—About 1 g. of the sample of the uncured or the cured mix was taken. The sample to be analysed must be very thinly sheeted in the case of uncured mix or powdered in the case of cured mix by passing through the tight nip of a rubber mixing mill. About 1 g. sample (cured or uncured) was wrapped with a clean filter paper (extracted with acetone), placed in an Underwriter's extraction cup, and extracted with acetone for 12 hours. The extract was distilled till about 20 c.c. of it was left in the flask. The distillate was transferred to a glass basin and evaporated to dryness on a water bath. The residue was redissolved in about 20 c.c. of ethanol and to it were added 3 drops of liquor ammonia and 3 drops of 20% strontium chloride solution in order to precipitate the fatty materials in the mix. The solution was filtered after keeping it overnight in the dark, washed with

ethanol, and made to 50 c.c. with ethanol in a volumetric flask. The above solution (10 c.c.) was treated similarly as in (*a*) for colour development and absorption measurement. Log absorbance against wave length was plotted and compared with those of the original antioxidants (Fig. 2).

FIG 1.

Absorption spectra of various antioxidants.

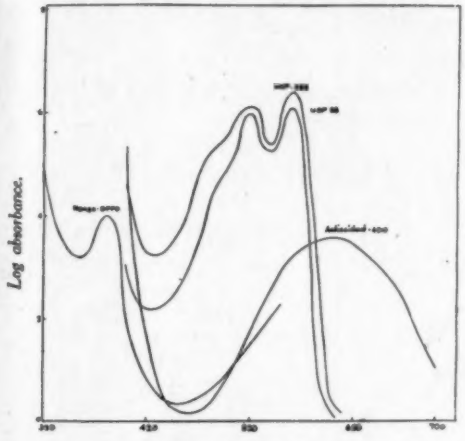
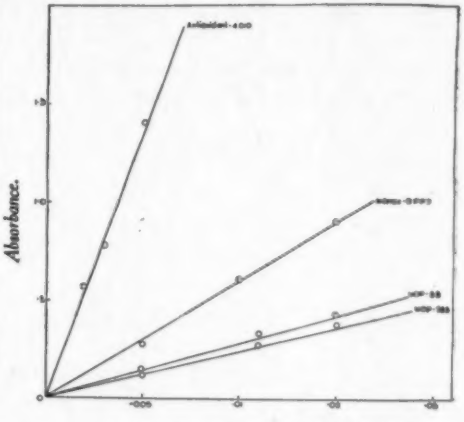


FIG 2.

Variation of absorbance against concentration.



This will give concentration of the antioxidant present in the extract whereas the wave length at maximum absorption will afford identification of the antioxidant. The visual colour of the oxidised solution of the anitoxidants in acidified ethanol is also characteristic and provides good indication for its identification.

Table II records the results of analysis of the antioxidants in the uncured and the cured mixes.

TABLE II

Stocks containing	Colour in acetic acid.	Colour developed after oxidation.	$\lambda_{max.}$	%Added (X).	%Found (Y).		Diff. (X-Y).	
					Uncured mix (A).	Cured mix (B).	X-A.	X-B.
Antioxidants 4010	Faint blue	Ultramarine blue	600mμ	1.20	1.08	1.05	0.12	0.15
					1.09	1.03	0.11	0.17
					1.11	1.04	0.09	0.16
Nonox DPPD	Nil	Ocean blue	380	1.61	1.58	1.52	0.03	0.09
					1.56	1.50	0.05	0.11
					1.58	1.49	0.03	0.12
UOP88	Red	Red colour deepens	560	1.35	1.31	1.28	0.04	0.07
					1.30	1.25	0.05	0.10
					1.32	1.27	0.03	0.08
UOP288	Do	Do	560	1.00	0.96	0.95	0.04	0.05
					0.97	0.95	0.03	0.05
					0.93	0.91	0.07	0.09

DISCUSSION

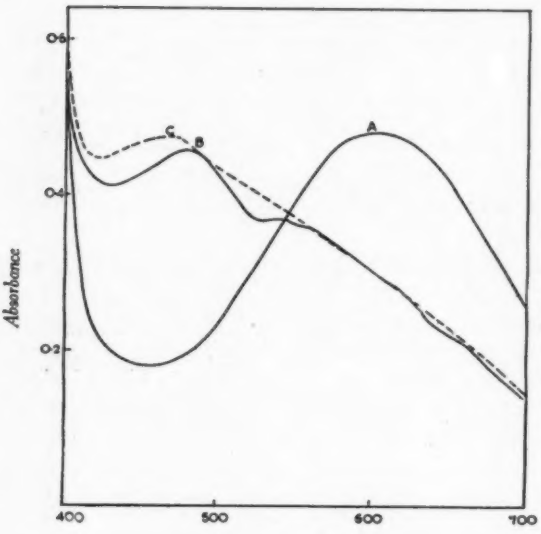
The results in Tables I and II indicate the feasibility of the present method in ascertaining the presence of a *p*-phenylenediamine derivative in an unknown sample of antioxidant as also of its identification provided that the absorption data are known from a previous study. The antioxidants present in an uncured or cured mix can also be identified and determined after extraction.

In the present study the antioxidants were determined within about 6 to 7% except in the case of antioxidant 4010, where the differences between quantity added and that found were higher (10 to 15%). The difference is higher in the case of the cured stock than in the uncured one, and the antioxidant found is always less than the quantity added. This is not unexpected as some antioxidant may be lost during extraction. Also there is a possibility of some quantity of antioxidant being consumed during curing at a high temperature; the loss by consumption explains higher figures in the case of cured stocks than uncured ones in the last two columns of Table II. It has also been observed that the usual compounding ingredients do not have appreciable effect on the determination*. Though analysis of the antioxidants is given in the range of 1 to 1.6% (Table II), the method is applicable to a much lower quantity.

An experiment with Acroflex CD (a mixture of phenyl-β-nappthylamine and diphenyl-*p*-phenylenediamine, DPPD) indicates the applicability of the present method to a mixture containing a *p*-phenylenediamine type of antioxidants as one of the components. The measured percentage of DPPD (36%) agrees well with the actual (35%). It seems that the colour formation, described above, is specific to this type. Other antioxidants like Nonox D, Nonox B, Nonox BL, Nonox HFN, Flectol H, Antioxidant MB, Nonox EXN, Nonox WSL, and Nonox KSM, do not give appreciable coloration with acidified permanganate solution. Even *p*-phenylenediamine itself does not exhibit any distinct colour under the specified condition (a yellow colour was obtained deepening with time). It was noted that ethanolic solutions of DPPD type of antioxidants, as found with a sample of antioxidant 4010, were oxidised by air even in stoppered bottles and developed the characteristic coloration of the oxidised samples on acidification alone. Further oxidation with permanganate changed the colour to violet and shifted the maximum absorption to shorter wave length, as was also observed in the case of oxidation with a large amount of permanganate (Fig. 3).

FIG. 3

Effect of $KMnO_4$ *conc. on the absorption spectrum of antioxidant* 4010.



Wave length ($m\mu$).

Concentration of $KMnO_4 = 2.5 \times 10^{-3}M$.

(A) 1.0 c.c. of $KMnO_4$/25 c.c. (B) 2.0 c.c. of $KMnO_4$/25 c.c.
(C) 2.5 c.c. of $KMnO_4$/25 c.c.

Thanks are due to Prof. S. K. Mukherjee and Prof. S. R Palit for encouragement during the course of this investigation.

* It may be noted here that the procedure of Hilton (*loc. cit.*) using cupric acetate as the oxidising agent is not applicable in presence of thiuram disulphide and thiocarbamate type of accelerators because of the formation of coloured cupric salts.

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Search for New Oral Hypoglycemic Agents. Part I. Synthesis of Some New Substituted Thioureas

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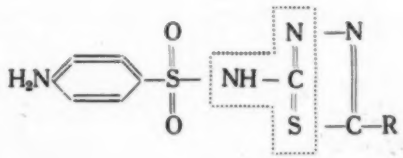
Several substituted thioureas have been prepared for testing their hypoglycemic activity.

Although the emergence of chemicals like Synthalin (Frank *et al.*, *Klin. Wochr.*, 1926, **5,** 2100), phenylethylformamidinyliminourea hydrochloride (Pcmcreuze *et al.*, *Proc. Soc. Exp. Biol.*, 1957, **95,** 193), carbutamide and tolubutamide (Franke and Fuchs, *Deutsh. med. Woch.*, 1955, **80,** 1449; Achelis and Hardebeck, *ibid.*, 1955, **80,** 1455), and 5-propyl^{i}-2-*p*-aminobenzenesulphanilamide-1, 3,4-thiadiazole (Janbon *et al.*, *Montpellier*, 1942, **21-22,** 489) undoubtedly points to the possibility of a positive chemotherapeutic approach to the problem of diabetes, a really potent antidiabetic agent remains yet to be discovered. Various theories put forward from time to time have so far not offered any definite clue as to the mode of action of hypoglycemic agents and in the present state of our knowledge it is difficult to pin-point an attack on this complex syndrome condition and to build effective antidiabetic compounds on a specific rationale. It can be noted, however, that most of the active antidiabetic compounds are built round a guanidine (e.g., synthaline and phenylethylformamidinyliminourea hydrochloride), a urea (e.g., carbutamide, tolbutamide, and chloropropamide), or a thiourea moiety [e.g., 5-propyl^{i}-2-*p*-aminobenzenesulphanilamide-1,3,4-thiadiazole-(I R = Pr^{i}) and 5-butyl^{n}-2-aminobenzenesulphonamide-1,3,4-thiadiazole (I : R = Bu^{n})].



(I)

In view of the above considerations several substituted thiourea derivatives have been prepared (*a*) by condensation of phenyl isothiocynate with γ-diethylaminopropyl^{n}amine, γ-piperidinopropyl^{n}amine, γ-morpholinopropyl^{n}amine, *p*-aminoacetanilide, *p*-aminoacetophenone, 3,5-dibromo-4-hydroxyaniline, sulphanilamide, sulphaguanidine, sulphathiazole, and sulphadiazine or (*b*) by

hydrolysing the 4-acetamidothiocarbanilide to 4-aminothiocarbanilide and subsequently allowing the resultant amine to react with *p*-toluenesulphonyl chloride, α-naphthalenesulphonyl chloride, β-naphthalenesulphonyl cholride, and benzyl chloride, or (*c*) by condensing phenyl isothiocyanate with *p*-chloroaniline and treating the resulting 4-chlorothiocarbanilide with γ-diethylamino-propyl^{n}amine, γ-piperidinopropyl^{n}amine, and γ-morpholinopropyl^{n}amine.

These thioureas have been characterised through their picrate in some cases.

EXPERIMENTAL

γ-Subsituted Aminopropyl^{n}amines.—γ-Diethylamino-, γ-piperidino-, and γ-morpholino-propyl^{n}amines were obtained by following the method of Weisel and Yanki (*J. Amer. Chem. Soc.*, 1944, **66**, 725).

Reactions of Phenyl Isothiocyanate

(*a*) *With Primary Aliphatic Amines.*—A mixture of phenyl isothiocyanate (0.05*M*) and one of the above mentioned amines (0.05*M*) in 95% ethanol (25 c.c.) was refluxed on a water bath for 6 hours. Ethanol was distilled and the resulting syrupy mass was kept over calcium chloride in a desiccator for 48 hours. The crystals of the substituted thioureas separating were filtered, washed, and recystallised from hot ethanol.

(*b*) *With Primary Aromatic Amines.*—Phenyl isothiocyanate (0.025*M*) was refluxed with aromatic amines (e.g., *p*-aminoacetanilide, *p*-aminoacetophenone or 3,5-dibromo-4-hydroxyaniline) (0.25*M*) in 95% ethanol (10 c.c.) for 15-20 minutes. The resulting thiourea derivatives were isolated as described above.

4-Chlorothiocarbanilide was prepared by the method of Kjellin (*Ber.*, 1903, **36**, 1076).

4-Ethoxycarbonylthiocarbanilide, reported earlier by Farooq and Hunter (this *Journal*, 1933, **10**, 465), was prepared by the above method in good yield.

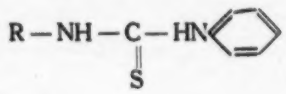
4-Aminothiocarbanilide, already reported by Lellmann and Wurtheur (*Annalen*, 1885, **228**, 218) was obtained by hydrolysing 4-acetamidothiocarbanilide with 20% HCl and then neutralising it with 20% NaOH; yield 70%, m.p. 219.

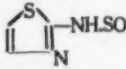
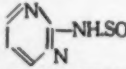
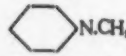
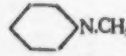
The duration of reaction for amines like sulphanilamide, sulphaguanidine, sulphathiazole, sulphadiazine was, however, found to be 7 to 8 hours and a little more of solvent was required to facilitate the reaction.

Condensation of 4-Aminothiocarbanilide with Chloro Compounds.—A mixture of 4-aminothiocarbanilide (0.25*M*) and each (0.05*M*) of *p*-methylphenylpsulphonyl chloride, α-and β-naphthalene-sulphonyl chlorides or benzyl chloride, and anhydrous potassium carbonate (0.25*M*) in ethanol (15 c.c.) was refluxed on a water bath for 7-8 hours in anhydrous condition. The substituted thioureas were extracted with hot ethanol and recrystallised from the same solvent (hot).

Condensation of 4-Chlorothiocarbanilide with Primarary Aliphatic Amines.—A mixture of γ-diethylamino-, γ-piperidino-, or γ-morpholino-propyl^{n}amine (0.003*M*) and 4-chlorothiocarbanilide (0.003*M*) in ethanol (5 c.c.) was refluxed on a water bath for 4 to 5 hours in anhydrous condition. The resulting thioureas being very hygroscopic could not be crystallised. These were characterised by preparing their picrates.

TABLE I



Sl. No.	R.	Thioureas. M.P.	Yield.	Formula.	%Nitrogen. Found.	Calc.	Picrates. M.P.	Yield.	Formula.	%Nitrogen. Found.	Calc.
1.	$CH_3CO.C_6H_4$-	142°	80%	$C_{15}H_{14}ON_2S$	10.10	10.60	..	..			
2.	$CH_3.CO\ NH.C_6H_4$-	213°	95	$C_{15}H_{15}ON_3S$	14.58	14.73	..	..			
3.	$HO.Br_2.C_6H_2$	168°	80	$C_{13}H_{10}N_2Br_2S$	7.11	7.25	..	..			
4.	$C_6H_5.NH.CS.HN.C_6H_4.SO_3$	116°	50	$C_{20}H_{18}O_3N_4S_3$	12.56	12.67	..	..			
5.		59°	55	$C_{16}H_{14}O_3N_4S_3$	14.28	14.35	..	..			
6.		83°	50	$C_{17}H_{16}O_3N_6S_2$	18.01	18.18	..	..			
7.	$C_6H_5NH.CS.HN.C$: (HN).$NH.SO_3.C_6H_4$-	65°	70	$C_{22}H_{20}O_3N_6S_3$	14.90	15.20	..	..			
8.	Et_2 : $N.CH_2C_6H_4CH_2.CH_3$-	106°	40	$C_{14}H_{23}N_2S$	17.02	17.14	..	..			
9.		126°	30	$C_{14}H_{21}ON_2S$	12.79	12.84	..	..			
10.		69°	35	$C_{13}H_{22}N_2S$	15.08	15.16	..	..			
11.	Et_2 : $N.CH_2.CH_2.CH_2.NH.C_6H_4$-	..	..	$C_{20}H_{28}N_4S$	..	..	156°	65%	$C_{26}H_{31}O_7N_7S$	16.74	16.75
12.		..	..	$C_{20}H_{26}ON_4S$	..	..	103°	60	$C_{26}H_{29}O_8N_7S$	16.29	16.39
13.		..	..	$C_{21}H_{28}N_4S$	..	..	>300° (d)	70	$C_{27}H_{31}O_7N_7S$	16.37	16.4° (d)
14.	α-$C_{10}H_7.SO_3.HN.C_6H_4$-	>300°	90	$C_{22}H_{19}O_3N_3S_2$	10.39	10.47	300° ..	50	$C_{28}H_{22}O_9N_6S_2$	13.22	13.3°
15.	β-$C_{10}H_7.SO_3.HN.C_6H_4$-	171°	85	$C_{22}H_{19}O_3N_3S_2$	10.41	10.47	300° ..	54	$C_{28}H_{22}O_9N_6S_2$	13.24	13.3°
16.	$CH_3.C_6H_4.SO_3.HN.C_6H_4$-	300°	85	$C_{20}H_{19}O_3N_3S_2$	11.44	11.50	300° ..	65	$C_{26}H_{22}O_9N_6S_2$	14.11	14.15
17.	$C_6H_5.CH_2.NH.C_6H_4$-	300°	90	$C_{20}H_{18}N_2S$	12.59	12.61	300° ..	72	$C_{26}H_{22}O_7N_6S$	14.90	14.97

An ethanolic solution of the resulting thiourea was heated on a water bath with an equal quantity of a saturated solution of picric acid in ethanol. On cooling, crystals of the respective picrates separated, which were recrystallised from hot ethanol.

The m.p., yields, and analytical data of the thioureas and their picrates obtained are recorded in Table I.

The authors are thankful to Dr. A. B. Sen, Professor and Head of the Chemistry Department, Lucknow University, for his interest in the present work.

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Fluoarsenates and Their Analogies with Sulphates. Part III*. Stability of Fluoarsenate Ion and its Comparison with Fluophosphate Ion

N. K. Dutt and Asim Gupta

Stabilities of fluophosphates and fluoarsenates have been measured by the method of Bjerrum and compared. K values of the reaction:

$$XO_3F^{2-} + H_2O = H_2XO_4^- + F^-$$

(where X = P or As) have been found as 5.2 and 5.61. Stabilities of these two complex acids have been found to be of the same order.

From our study of the various compounds (simple, double, and basic) of fluoarsenates (*Z. anorg. allgem. Chem.*, 1956, **285**, 92; this *Journal*, 1960, **37**, 805) of bivalent metals, these appear to be as stable as the corresponding flouophosphates. A study of the stabilities of these ions has therefore been deemed desirable. The present paper describes the comparison of the stabilities of the fluophosphates and fluoarsenates in solution.

The principle utilised in the study is the theoretical relationship outlined by Bjerrum ("Metal Ammine Formation in Aqueous Solution", Haase and Son, 1941) in the change of *p*H due to complex formation on a statistical basis involving all the possible intermediate stages in a reversible manner. These relationships are not restricted to complex formation only, but may be applied to any equilibrium process regardless of the nature of the reacting substances.

For this study, the dissociation constants of H_3AsO_4, H_3PO_4, and HF having been considered necessary were determined following the method of Bjerrum by plotting $\bar{n}$ against the *p*H values of the solutions resulting from progressive addition of standard acid to solution of known strength of normal salts of either H_3AsO_4 or H_3PO_4 and anhydrous NaF.

* Part II : This *Journal*, 1960, **37**, 805.

Decompositions of Monofluophosphate and Monofluoarsenate Ions in Aqueous Solution

The above ions may be assumed to react with acid in aqueous solution in the following manner:

$$[XO_3F]^{2-} + H^+ \rightleftharpoons [HXO_3F]^- \quad .. \quad (1)$$

$$[HXO_3F]^- + H^+ + H_2O \rightleftharpoons H_3XO_4 + HF \quad .. \quad (2)$$

where X stands for P or As. The respective equilibrium constants are:

$$K_1 = \frac{[HXO_3F]^-}{[XO_3F]^{2-}\ [H^+]}$$

$$K_2 = \frac{[H_3XO_4]\ [HF]}{[HXO_3F]^-\ [H^+]}$$

K_1 and K_2 were determined in the following way as the reactions took place in a stepwise manner.

The *p*H values were measured at successive stages when a standard acid was added progressively to solutions of the salts of known strength.

If C represents the molar concentration of $[XO_3F]^{2-}$ originally taken, C_0, that of $[XO_3F]^{2-}$ at equilibrium, and C_1, that of $[HXO_3F]^-$ at equilibrium.

$\therefore\ C = C_0 + C_1 + H_3XO_4 + H_2XO_4^- + HXO_4^{2-}$ (for all purposes XO_4^{3-} has not been taken into consideration).

$$C = C_0 + C_1 + F^- + HF.$$

A (acid added) $= C_1 + H_3XO_4 + HF - HXO_4^{2-} - OH^- + H$ (acid left).

$A + OH^- - H$ (acid consumed) $= H_3XO_4 + HF - HXO_4^{2-} + C_1$.

There are two possible cases depending on the relative values of $(A + OH^- - H)$ and C.

(1) $C > A + OH^- - H$ where reaction (2) above is considered not to have taken place when $C = C_0 + C_1$.

$$A + OH^- - H = C_1$$

and

$$K_1 = \frac{C_1}{C_0 \times [H^+]} = \frac{[A + OH^- - H]}{[C - (A + OH^- - H)]\ [H^+]}.$$

(2) $A + OH^- - H > C$, when C_0 is considered to be zero, where

$$C = C_1 + H_3XO_4 + H_2XO_4^- + HXO_4^{2-}$$

$$C = C_1 + F^- + HF$$

$$A + OH^- - H = HF + H_3XO_4 - HXO_4^- + C_1 \quad .. \quad (3)$$

$$K_2 = \frac{[H_3XO_4]\ [HF]}{[H^+]\ C_1}$$

and from the knowledge of the first two dissociation constants of H_3XO_4 (k' and k'') and that of HF (k_1)

$$= \frac{[H^+]\ [C - C_1]^2}{C_1(k' + H)\ (k_1 + H)}$$

where $C_1 = (A + OH^- - H)\,HF - H_3XO_4 \left(\frac{1 - k'k''}{H^2}\right)$ from (3)

$$= \frac{C\,[2H^3 + H\,(k_1k')] - (A + OH^- - H)\,(k_1 + H)\,(k' + H)}{H^3 - k_1k'}$$

Overall Stability or Decomposition Constant

From the stepwise decompositions of $[XO_3F]^{2-}$ by progressive addition of acids, the overall equation becomes (adding eqns. 1 and 2)

$$[XO_3F]^{2-} + 2H^+ + H_2O \rightleftharpoons H_3XO_4 + HF$$

$$\text{where } K \text{ (overall)} = \frac{[H_3XO_4]\,[HF]}{[XO_3F]^{2-}\,[H^+]^2}$$

$$= \frac{[H_3XO_4]\,[HF]}{[HXO_3F]^-\,[H^+]} \times \frac{[HXO_3F]^-}{[H^+]\,[XO_3F]^{2-}}$$

$$= K_1K_2.$$

Now from the above values we can calculate the constant for the following reaction as shown :

$$[XO_3F]^{2-} + H_2O \rightleftharpoons H_2XO_4^- + F^-$$

as shown :

$$K_h \text{ (hydrolytic)} = \frac{[H_2XO_4]^-\,[F^-]}{XO_3F]^{2-}}$$

which can be broken up and written as

$$= \frac{[H_3XO_4]\,[HF]}{[XO_3F]^{2-}\,[H^+]^2} \cdot \frac{[H^+]\,H_2XO_4]^-}{[H_3XO_4]} \cdot \frac{[H^+]\,[F^-]}{[HF]}$$

$$= K_1K_2k_1k'.$$

EXPERIMENTAL

The hydrogen-ion concentrations were measured with a Phillips *p*H-meter, model No. GM 4491 using a quinhydrone electrode and a saturated calomel electrode. Glass portions of the electrodes were coated with paraffin. A polyethylene beaker was used as the titration vessel. For uniform mixing of the reacting liquids, a paraffin-coated electric stirrer was used. All solutions were prepared using a molar potassium chloride solution. While titrating, sufficient quantity of quinhydrone was added to the solutions.

K_2AsO_3F was prepared as described previously (*loc. cit.*, 1956). K_2PO_3F was prepared as described by Boothe ("Inorganic Synthesis", Vol. II, pp. 155-56, 1946). All other reagents used were of AnalaR quality.

TABLE I

Dissociation constants.

	H_3PO_4.	H_3AsO_4.	HF.
k'	1×10^{-2}	1.1×10^{-2}	
k''	4×10^{-7}	2.0×10^{-7}	
k_1	..	..	3.16×10^{-4}

TABLE II

Dissociation studies of $K_2[PO_3F]$ *and* $K_2[AsO_3F]$.

A.	H.	C.	C_1.	C_0.	K_1.	K_2.	Mean.
		A. $K_2PO_3F = 0.0119M$. HCl = 0.5*M*.					
4.90×10^{-4}	$1.4^{\circ} \times 10^{-7}$	1.180×10^{-2}	5.2×10^{-4}	1.13×10^{-2}	1.6×10^{5}		
9.90×10^{-4}	3.53×10^{-7}	1.175×10^{-2}	1.2×10^{-3}	1.08×10^{-2}	1.3×10^{5}		
1.49×10^{-3}	6.10×10^{-7}	1.170×10^{-2}	1.5×10^{-3}	1.03×10^{-2}	1.2×10^{5}		
2.50×10^{-3}	9.50×10^{-7}	1.165×10^{-2}	2.5×10^{-3}	9.30×10^{-3}	1.4×10^{5}		
3.50×10^{-3}	1.62×10^{-6}	1.160×10^{-2}	3.5×10^{-3}	8.30×10^{-3}	1.3×10^{5}		
3.90×10^{-3}	2.04×10^{-6}	1.150×10^{-2}	3.9×10^{-3}	7.90×10^{-3}	1.2×10^{5}		2.66×10^{5}
2.15×13^{-3}	6.16×10^{-3}	1.140×10^{-2}	1.03×10^{-3}	1.04×10^{-2}		6.16	
2.38×10^{-3}	$8.1^{\circ} \times 10^{-3}$	1.130×10^{-2}	9.8×10^{-4}	1.03×10^{-2}		5.55	
2.60×10^{-3}	$9.8^{\circ} \times 10^{-3}$	1.125×10^{-2}	9.7×10^{-4}	1.02×10^{-2}		5.12	5.61
		B. $K_2AsO_3F = 0.01025M$. HCl = 0.5*M*					
$5.9^{\circ} \times 10^{-4}$	9.33×10^{-8}	1.024×10^{-2}	5.90×10^{-4}	9.65×10^{-3}	6.5×10^{5}		
$9.9^{\circ} \times 10^{-4}$	1.32×10^{-7}	1.023×10^{-2}	9.90×10^{-4}	9.24×10^{-3}	8.1×10^{5}		
1.49×10^{-3}	1.74×10^{-7}	1.022×10^{-2}	1.49×10^{-3}	8.73×10^{-3}	9.8×10^{5}		
3.47×10^{-3}	7.08×10^{-7}	1.018×10^{-2}	3.47×10^{-3}	6.71×10^{-3}	7.3×10^{5}		
4.90×10^{-3}	1.78×10^{-6}	1.015×10^{-2}	4.90×10^{-3}	5.25×10^{-3}	5.24×10^{5}		7.40×10^{5}
2.38×10^{-2}	9.55×10^{-3}	9.760×10^{-3}	1.62×10^{-3}	8.74×10^{-3}		2.00	
2.60×10^{-2}	1.10×10^{-2}	9.700×10^{-3}	1.46×10^{-3}	8.25×10^{-3}		2.22	
2.82×10^{-2}	1.35×10^{-2}	9.670×10^{-3}	1.17×10^{-3}	8.50×10^{-3}		2.31	2.18

	K_2PO_3F.	K_2AsO_3F.
Overall const. $K = K_1K_2$	1.49×10^{5}	1.61×10^{5}
Hydrolytic const. $K_h = K_1K_2k_1k'$	5.2	5.61

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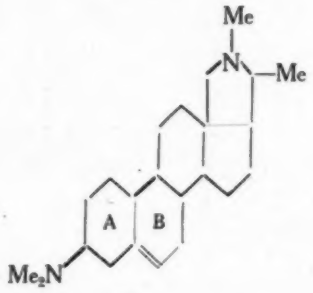
Search for New Amoebacides. Part V. Synthesis of Indan-pyrrolidines

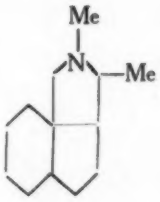
K. L. Pathak and B. Pathak

A few *N*-alkylated indan-pyrrolidines have been prepared by $LiAlH_4$ reduction of indane 1,2-dicarboxy-*N*-alkyl imides with the object of testing their amoebacidal activity.

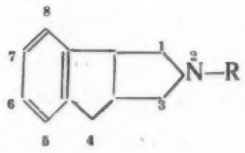
Conessine (I), a steroidal alkaloid present in *Holarrhena antidysenterica* (Indian Kurchi) possesses antiamoebic activity. If the rings A and B are abolished in conessine, it leads to a hexahydroindan-pyrrolidine of the type (II,) which was named by Haworth and Michael (*J. Chem. Soc.*, 1957, 4973) as dihydro-*des*-AB-con-8-eine. Little work appears to have been done on indan-pyrroles and indan-pyrrolidines. Syntheses of indan-pyrrolidines of type (III) have therefore been undertaken to ascertain their amoebacidal activity. Winans and Adkins (*J. Amer. Chem. Soc.*, 1933, **55,** 4167) reported formation of 2-methyl-3-ethoxycarbonyl-4,5-indenopyrrole by the interaction of isonitrosohydrindone and ethyl acetoacetate under high pressure hydrogenation in presence of Ni-catalyst. Bondietti and Lions (*J. Proc. Roy. Soc., N. S. Wales*, 1933, **66,** 477) reported a synthesis of 2-methyl-3-acetyl-4,5-indeno-1,2-pyrrole.



(I)

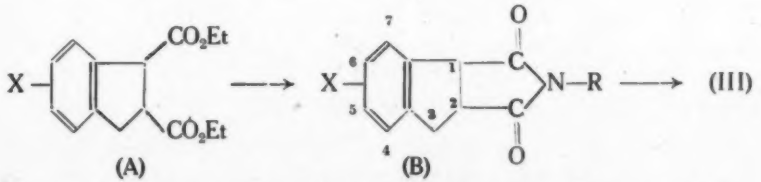


(II)



(III)

Indan-pyrrolidines (III) have been synthesised on the following route :



Ethyl indene-1,2-dicarboxylate (Bougault, *Compt. rend.*, 1914, **159,** 745) and its 5,6-dimethoxy derivative (Horning *et al.*, *J. Amer. Chem. Soc.*, 1951, **73**, 5826) were hydrogenated in presence

of Ni-catalyst. Indan-dicarboxy esters (A), thus formed, were heated with an appropriate alkylamine to yield imides (B). A portion of the reaction product always yielded diamide, which on further heating did not yield imide; it was considered to be a *trans*-diamide. The imides have been smoothly reduced by $LiAlH_4$ to the desired indan-pyrrolidines (III).

EXPERIMENTAL

Ethyl Indan-1,2-dicarboxyate (A : X = H).—Ethyl indene-1,2-dicarboxylate was hydrogenated in presence of Raney nickel, b.p. 160-62°/2.4 mm.

Ethyl indan-5,6-dimethoxy-1,2-dicarboxylate (A : X = 5,6-OMe) was prepared by hydrogenation of the corresponding indene. It was crystallised from petroleum ether (60-80°), m.p. 91-92°.

Indan-1,2-dicarboxy-N-alkylimide (B).—Indan-1,2-dicarboxy ester (0.02 *M*) was heated with a primary alkylamine (0.1*M*) in a sealed tube in a water bath or in an oil bath (150°) for 8 hours. On removal of excess amine the product was heated till the amine had ceased to evolve. The imide was recovered by either crystallisation from hot water or by extraction with petroleum ether (60-80°) and subsequent distillation of the extract. Table I shows the characteristics of different imides.

TABLE I

R.	Method of recovery.	M.P./B.P.	Formula.	%Nitrogen. Found.	%Nitrogen. Calc.	M.P./B.P.	Formula.	%Nitrogen. Found.	%Nitrogen. Calc.
			B : X = H.				B : X = 5,6-OMe.		
Me	a	71-72°	$C_{12}H_{11}O_2N$	6.6	6.8	120-22°	$C_{14}H_{15}O_4N$	5.1	5.3
Et	a	78-80°	$C_{13}H_{13}O_2N$	6.3	6.4	119-20°	$C_{15}H_{17}O_4N$	5.2	5.0
Pr^n	b	155-58°/1mm	$C_{14}H_{15}O_2N$	5.7	6.0	84-86°	$C_{16}H_{19}O_4N$	5.0	4.8
Bu^n	b	170-74°/0.6	$C_{15}H_{17}O_2N$	5.8	5.7	215-17°/0.5mm	$C_{17}H_{21}O_4N$	4.6	4.6
$Amyl^n$	b	195-97°/3.5	$C_{16}H_{19}O_2N$	5.6	5.4	230-32°/3.5	$C_{18}H_{23}O_4N$	4.3	4.4

(a) By crystallisation from hot water.
(b) Extracted with pet. ether (60-80°); ether was removed and the residual liquid was distilled *in vacuo*.

Indan-1,2-dicarboxy-N-methylimide was also prepared in a different manner. Indan-1,2-dicarboxy ester on heating with liquor ammonia in a sealed tube afforded imides in poor yield. The latter was crystallised from hot water, m.p. 170-72°. (Found : N, 7.6. $C_{11}H_9O_2N$ requires N, 7.4%).

N-*Potassio-derivative* was prepared in quantitative yield by addition of ethanolic KOH to the imide solution in ethanol. Potassio-derivative of the imide on heating in benzene solution with excess of methyl iodide on a water bath for 8 hours yielded *N*-methyl compound in good yield (80%), proved identical with that prepared by the previous method.

Indan-N-alkylpyrrolidine (III).—Indan-1,2-dicarboxy-*N*-alkylimide was reduced with $LiAlH_4$ in dry ether. Pyrrolidine was then recovered by extraction of the ether solution with HCl (dil.). The latter was basified with NaOH solution and extracted with ether. The ether solution was dehydrated and distilled. Table II shows characteristics of different compounds.

TABLE II

R.	B.P.	Picrates. M.P.	Formula.	%Nitrogen. Found.	Calc.	Hydrochlorides. M.P.	Formula.	Found.	Calc.
				III : X = H.					
Me	104-106°/1.7 mm	188-90°	$C_{15}H_{15}O_7N_4$	13.6	13.9	125°	$C_{13}H_{16}NCl$	C : 68.5 H : 8.0	68.7 7.6
Et	104-106°/0.7	179-80°	$C_{19}H_{20}O_7N_4$	13.2	13.4	145°	$C_{13}H_{18}NCl$	C : 69.7 H : 8.2	69.8 8.0
Pr^n	115-17°/0.6	170-72°	$C_{20}H_{22}O_7N_4$	13.0	13.0	120°	$C_{14}H_{20}NCl$	C : 70.4 H : 8.7	70.7 8.4
Bu^n	122-25°/0.6	174-76°	$C_{21}H_{24}O_7N_4$	12.4	12.6	158°	$C_{15}H_{22}NCl$	C : 71.8 H : 9.0	71.6 8.7
Am^n	150-52°/3.5	147-49°	$C_{22}H_{26}O_7N_4$	11.9	12.2	..			
				III : X = 6,7-OMe.					
Me	155-58°/1.5 mm	192-94°	$C_{20}H_{22}O_9N_4$	11.9	12.1	164°	$C_{14}H_{20}O_2NCl$	C : 62.1 H : 7.6	62.3 7.4
Et	155-57°/0.8	175-76°	$C_{21}H_{24}O_9N_4$	11.6	11.7	213°	$C_{15}H_{22}O_2NCl$	C : 63.1 H : 7.9	63.5 7.7
Pr^n	160-62°/1.5	182-84°	$C_{22}H_{26}O_9N_4$	11.2	11.4	161°	$C_{16}H_{24}O_2NCl$	C : 64.2 H : 8.2	64.5 8.0
Bu^n	168-70°/0.6	162-64°	$C_{23}H_{28}O_9N_4$	10.8	11.1	162°	$C_{17}H_{26}O_2NCl$	C : 65.2 H : 8.5	65.5 8.4
Amyl^n	160-62°/0.6	166-68°	$C_{24}H_{30}O_9N_4$	10.7	10.8	..			

The authors desire to express their deep appreciation to the Ministry of Scientific Research and Cultural Affairs, Government of India, and to Sri B. Bhattacharyya, Department of Chemistry, for the grant of chemicals and for microanalysis respectively.

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SHORT NOTES

Reaction of Grignard Reagents with Heterocyclic Compounds

A. B. Lal

Bergostrom and McAllister (*J. Amer. Chem. Soc.*, 1930, **52,** 2845) obtained 2-alkyl- or 2 aryl-pyridines or quinolines by the action of ethyl- or phenylmagnesium bromide on pyridine or quinoline. Goetz-Luthy (*ibid.*, 1949, **71,** 2254) failed, however, to isolate any 2-ethylpyridine and found that ethylmagnesium bromide with pyridine gave, presumably, a small quantity of dipyridyl, but most of the pyridine was recovered unchanged.

The action of the Grignard reagents on the 2-, 3-, or 4- picoline and quinaldine does not appear to have been reported, although the activity of the hydrogen atoms of the methyl group is well known. Thus Levine *et al.* (*ibid.*, 1951, **73,** 4301) found that 2-picoline was converted to its lithium derivative by the action of phenyllithium. It has now been found that addition of ethereal solutions of 2-, 3-, or 4- picoline or quinaldine to a solution of phenylmagnesium bromide (in ether) results in the formation of a white precipitate. This immediately dissolves in all cases except in the case of 4-picoline. The colour of the solution turns red in all cases. The reaction with pyridine also gave an insoluble white precipitate but not with quinoline. In the latter case, the ethereal solution deposited colorless cubic crystals on cooling. This is quite different from that reported by Gilman (*ibid.*, 1949, **71,** 2327).

The precipitates were obtained in nearly quantitative yield. That from 4-picoline appeared to be more stable than the one from pyridine, but both decomposed when left exposed to air. In a desiccator these did not decompose. The precipitates reacted vigorously with water leaving a small residue and the original heterocyclic compound. The cubic crystals behaved in a similar manner. None of these had any definite melting point, but these melted over a wide range of temperature. The nature of these complexes is being investigated.

Among the reaction products diphenyl was identified. The quantity of this product varied in each case, but was always less than that expected. This was verified by refluxing an ethereal solution of phenylmagnesium bromide under the same conditions as that under which the reactions were carried out. A preliminary investigation of the reaction products revealed that substitution in the side chain of the heterocyclic compounds did not occur. Only in the case of 2-picoline, a small quantity (3%) of a base was obtained which reacted with methyl iodide to afford a substance quite different from 2-picoline methiodide (chars at $> 200°$ and m.p. 250°).

Gilman (*ibid.*, 1957, **79,** 1245; 1959, **81,** 4000) has reported the reaction between allylmagnesium bromide and some heterocyclic compounds. The action of this reagent on picolines and 4-methylcinnoline has now been studied. It appears that the reaction took place in all cases where the 2-position was free. Thus 2-picoline and 2,6-lutidine do not appear to react. White or yellowish precipitates, similar to those described above, were also obtained. Further work is in progress and will be reported in another communication.

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On *o*-Nitrocinnamaldehyde

P. John Jacob and P. I. Ittyerah

This note deals with the observations made during the condensation of *o*-nitrocinnamaldehyde with malonic, malonanilic, malon-*o*-,-*m*- and -*p*-toluidic and malon-*o*-chloranilic acids. A trace of an organic base like pyridine, piperidine or 2,4-lutidine, or of a salt like pyridine acetate or molecular proportions of glacial acetic acid was used in these experiments as a condensing agent.

Condensation with malonic acid furnished two products—one melting at 205° and the other at 216°. The latter was identified as *o*-nitrocinnamylidene-acetic acid. The lower melting product is taken to be *o*-nitrocinnamylidene-malonic acid, but this needs further confirmation. In all other cases only one type of product, viz., *o*-nitrocinnamylidene-malonanilic, -toluidic, or -chloranilic acid, was obtained. The other expected product, viz., *o*-nitrocinnamylidene-acetanilide,-toluidide, or -chloranilide, was not isolated in any reaction. This is in agreement with the observations made by Bagchi and Ittyerah (*Agra Univ. J. Res.*, 1954, **3**, 143) in the reactions of cinnamaldehyde.

It was further noted that in all reactions, except with that of malonic acid, *o*-nitrocinnamaldehyde showed greater reactivity than the unsubstituted aldehyde. Mention may be made here that attempts to condense hydrocinnamaldehyde with the reactive methylene compounds, named before, were unsuccessful.

The general procedure involved the mixing of the aldehyde (1 *M*), acid (1*M*), and the catalyst (0.15 *M*) in a r.b. flask and heating the mixture at 100-105° for 4 hours. The solid left was extracted with a strong solution of sodium carbonate. The alkali extract on addition of excess of HCl gave the product, which could be further purified by recrystallisation from ethanol. When acetic acid was used as a condensing agent, it was added in molecular proportions. The two products obtained in malonic acid condensation could be separated by ether, *o*-nitrocinnamylideneacetic acid being soluble and the other component insoluble.

TABLE I

No.	Name.	Formula.	M.P.	%Yield.	%Nitrogen. Found.	Calc.
1.	*X-acetic acid	$C_{11}H_9O_4N$	216°	64	6.11	6.39
2.	X-malonanilic acid	$C_{18}H_{14}O_3N_2$	185°	89	8.83	8.29
3.	X-malon-*o*-toluidic acid	$C_{19}H_{16}O_3N_2$	217°	51	8.10	7.95
4.	X-malon-*m*-toluidic acid	$C_{19}H_{16}O_3N_2$	212°	56	7.87	7.95
5.	X-malon-*p*-toluidic acid	$C_{19}H_{16}O_3N_2$	225°	86	8.4	7.95
6.	X-malon-*o*-chloroanilic acid	$C_{18}H_{13}O_3N_2Cl$	228°	67	7.78	7.66

*X-stands for *o*-nitrocinnamylidene.

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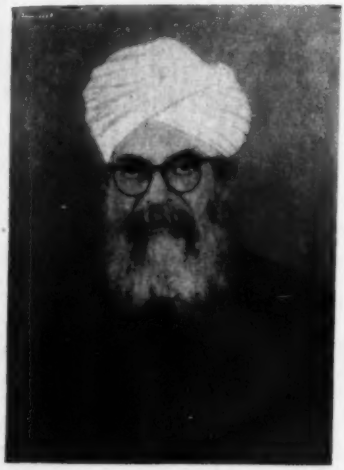
OBITUARY

Bawa Kartar Singh

Born : April 17, 1886. Died : June 16, 1960.

Bawa Kartar Singh, one of the pioneers in stereochemical researches in India, breathed his last on June 16, 1960 at Chandigarh, Punjab. Though frail in body he nestled a vigorous mind within, even at seventies. He was the surviving son of Col. B. J. Singh, I. M. S., Inspector General of Prisons, Govt. of India, his other two brothers being the victims in the tragic loss of Lousitania by enemy submarine during World War I.



He was born on April 17, 1886 at Verowal, Amritsar Dist. of the Punjab. He was a direct descendant of the 3rd Sikh Guru and was himself a staunch devotee of his religious order. He began his study at the D.A.V. School at Lahore but soon after, on account of the transfer of his father to Burma, he was admitted at the Rangoon Collegiate School from where he passed the Entrance (now School Final) examination under the Calcutta University in 1903, standing seventh in order of merit. He proceeded to England in 1904 to prosecute his higher studies at the Downing College of the Cambridge University where he distinguished himself as a Prizeman of the College in 1905 and carried the distinction further by obtaining Tripos in Natural Sciences in 1906. During 1906-1910 he prosecuted his post-graduate studies in the Universities of Cambridge and London. He was awarded Sc.D. degree by the Dublin University in 1921 for his researches in stereochemistry of camphor derivatives.

On his return to India in 1910, B. K. Singh joined the Dacca Govt. College as the Professor of Chemistry. Here he came in intimate contact with Late Dr. E. R. Watson, the reputed dye chemist of India, and the first Hony. Editor of the Indian Chemical Society. Under the inspiration of Dr. Watson, he began his researches on optically active nitrogen compounds at the ill-equipped College laboratory. He left Dacca College in 1918 to join the Govt. College, Lahore, as the Head of the Department of Chemistry. Soon after, with ardent zeal and perseverance, he was able to create an atmosphere of active research in his Department. In 1921 he was selected for appointment in the I.E.S. and was posted at the Patna Govt. College (now Patna University) but only to be transferred after six months to the Ravenshaw College, Cuttack. Here he stayed as the Head of the Department of Chemistry till 1936. In spite of the meagre facilities for research in the College, Dr. Singh carried on researches in his favourite lines and published a large number of papers in scientific journals in India and abroad.

During 1925-26, Dr. Singh went to England and France on study leave and worked in the Universities of Cambridge, St. Andrews, and Paris. Soon after his return to Cuttack, he attracted the attention of the scientific world to his brilliant researches on stereochemistry of camphor compounds.

While at Lahore, Dr. Singh was elected the President of the Chemistry Section of the Indian Science Congress in 1920. He was also elected the President of the Lahore Philosophical Society and a Fellow of the Punjab University in the same year. He was a Foundation Fellow of the Indian Chemical Society, serving the Society since its inception under various capacities as Member of the Council, Hony. Editor, Vice-President and President (1931-32). Dr. Singh was also actively associated with other scientific bodies of India. He was elected Vice-President of the Indian Academy of Sciences during 1934-1938 and additional Vice-President of the National Institute of Sciences of India for two terms. He also acted as the Foreign Secretary of the National Academy of Sciences of India during 1944-46, while at Allahabad. In 1936 Dr. Singh again came to Patna as the Head of the Chemistry Department of the Science College under the Patna University and as the Chemical Adviser to the Department of Industries, Govt. of Bihar. He stayed there till the middle of 1940. Up to this time he had to his credit no less than fifty research papers published in various scientific journals. After retirement from Government Service, he joined the Allahabad University in 1940 as the Professor and Head of the Department of Chemistry. After his retirement in 1946, he was appointed an Emeritus Professor of Chemistry by the Allahabad University.

Dr. Singh now decided to settle at Lahore and pursue his researches in chemistry and Sikh sagas (one of his favourite recreations). For this purpose he bought a piece of land for building a house at Model Town, Lahore, and asked the Punjab University for research facilities, which were readily granted. He was forthwith appointed as an Hony. Professor of Chemistry and an Associate Director of the Punjab Institute of Chemistry. But fate willed otherwise. The tragic partition of India compelled him to quit his native province. Ultimately Banaras Hindu University offered him research facilities and he settled at Varanasi in 1948 to pursue his favourite avocation till death snapped it. During his stay at Banares, in collaboration with his students he published more than 40 papers. There are no less than a hundred published papers to his credit devoted mainly to the various aspects of optical activity of organic compounds. He also engaged himself in writing in collaboration with the author, a monograph on 'Optical Activity and Chemical Constitution'—a project sponsored by U.P. Scientific Research Committee in November 1959.

He had an attack of paralysis at the age of 74, but he never contemplated absolute retirement from active research. As a matter of fact he was awarded a grant for 1960-61 by C.S.I.R. and this he decided to utilise for his further researches at Chandigarh under the Punjab University till death cut short his long research life of nearly half a century.

Dr. Singh was most unassuming, a hard task master and very friendly with his students. May his soul remain in peace !

O. N. Perti.

Mahendra Nath Goswami

Born : 1894. Died : Feb. 9, 1961.

Dr. Mahendra Nath Goswami, formerly Professor in the Department of Applied Chemistry, University College of Science and Technology, Calcutta University, died suddenly on February 9, at his Calcutta residence. He is survived by his widow, four sons and a daughter.

Dr. Goswami had his early education in Cooch Behar and Dacca. After taking his M.A. from the Presidency College, Calcutta, in 1918, he worked for some time as a chemist at the Government Excise Laboratory at Kanpur. He took up teaching as his profession and served Ripon (now Surendranath) College for two years.

He joined the Department of Applied Chemistry, University College of Science & Technology, Calcutta, in 1921.

Dr. Goswami proceeded to France in 1924 to work under the eminent scientist, Dr. Paul Sabatier at the latter's Research Institute at the University of Toulone and received the Doctorate degree after submitting a thesis on "Direct hydrogenation and dehydrogenation of acenaphthene", expounding the behaviour of reduced Nickel as a catalyst. During his stay in Europe, Dr. Goswami visited many industrial concerns to gain first hand knowledge of large-scale production technique.

On his return to India in 1926, he was appointed a Lecturer in the Department of Applied Chemistry, Calcutta University. He served the Department for a long period of 33 years during which time the activities of the Department increased enormously, and Dr. Goswami had a significant contribution towards this development. He acted as the Head of the Department for the periods 1944-47 and 1949-52. He took an active part in most of the planning work for the development of the Department. In 1953, Dr. Goswami was appointed a Reader in Applied Chemistry.

During the period of his service, Dr. Goswami carried out with his associates a series of important works on synthetic organic chemistry, organo-arsenic compounds, catalysis and on problems relating to oil, fuel, and carbohydrate industries.

Among the more important contributions which he has made in organic chemistry are :

(1) Stability of unsaturated organic compounds in presence of nickel catalysts at higher temperatures.

(2) Synthesis of benzopyrylium compounds.

(3) Catalytic oxidation of paraffins.

(4) Intradehydration of ether and ammonia in presence of catalysts for the preparation of alkylanilines.

(5) Introduction of arsenic into coumarin nucleus by modified Bart's reaction.

Among a number of analytical methods, which he developed, mention may be made of : (*i*) Use of Nessler's reagent for the quantitative determination of monosaccharide, disaccharide, furfural, formaldehyde, pyrogallol, tannic and gallic acids, (*ii*) rapid method of determination of unsaturation in organic compounds, particularly oils, with hypochlorous acid.

Dr. Goswami's researches in the domain of fixed oils and essential oils have been extensive. Mention may be made of (*i*) selective alcoholysis of oils, (*ii*) synthesis of ring glycerides, (*iii*) investigation into chemical changes during the processing of boiled oils, (*iv*) investigation into the causes of sweating of soaps, (*v*) investigation into the causes of rancidity of fats, and (*vi*) hydrogenation of fatty acid salts in water solutions at ordinary temperature and pressure.

In the field of essential oils he studied the oleoresin of *Boswellia serrata* and preparation of geraniol and geraniol esters in detail.

Dr. Goswami was a pioneer in carrying out research on plastics in this country. In 1938 he worked out a process for the manufacture of thermoplastic resins from vegetable oils which was later patented and also made an exhaustive study on the methods for preparation of cellulose acetate and viscose.

On fuels his main investigations concerned the desulphurization of Indian coals.

Dr. Goswami may also be called a pioneer in the field of industrial chemistry. He has a number of patents to his credit. His work on splitting of vegetable oils and his report on the commercial possibility of the manufacture of lactose have been published by the Department of Commerce, Govt. of India and the Department of Industries, Govt. of West Bengal, respectively. As a practical perfumer and an expert on the blending of perfumes, his advice was sought by many.

As a teacher, Dr. Goswami was very strict though affectionate towards his students. He had a very good experimental hand and even in his advanced age he would demonstrate experimental procedures to students and research workers. As a hard task master he spared neither himself nor others. Outside the class rooms and laboratories he was a jovial man with a fund of humour. His love for the teaching profession was so much that he could not be lured into other remunerative jobs which were offered to him many times.

In his death the country has lost a brilliant industrial chemist, a veteran educationist, and a great teacher.

M. M. Chakravarti.

REVIEWS

Technique of Organic Chemistry. Vol. I. Physical Methods of Organic Chemistry. Part I. Edited by Arnold Weissberger. Interscience Publishers Inc., New York, U.S.A. Third edition. 1959. Pages 918 + xii. Price $24.50.

The expansion of Volume I of this exceedingly useful series on the Technique of Organic Chemistry will be most welcome to chemists in general and to organic chemists in particular who are becoming increasingly dependent upon physical methods for tackling their problems.

Four new topics have been incorporated in Part I, viz., "Automatic Control" by J. M. Sturtevant, "Automatic Recording" by D. R. Simonsen, "Weighing" by A. Corwin, and "Determination of Particle Size and Molecular Weight" by G. B. Beyer. Five chapters belonging to Part I of Ed. 2 have been transferred to Part II. These are "Determination of Diffusivity", "Determination with the Ultracentrifuge", "Microscopy", "Determination of Crystal Form", and "Crystallochemical Analysis". The topic on "Temperature Control" has been incorporated in the chapter on "Automatic Control".

The following chapters have been retained from Part I of Ed. 2 : "Determination of Density", "Temperature Measurement", "Determination of Melting and Freezing Temperatures", "Determination of Boiling and Condensation Temperatures", "Determination of Vapour Pressure", "Calorimetry", "Determination of Solubility", "Determination of Viscosity", "Determination of Properties of Insoluble Monolayers at Mobile Interfaces" (Change of title), "Determination of Surface and Interfacial Tension", "Determination of Osmotic Pressure".

The original plan of presentation, viz., discussion of the fundamentals, types of apparatus used, precision and accuracy of the method, and its comparison with other techniques, wherever possible, has been adhered to. A useful bibliography has been given at the end of each chapter.

While the accuracy of a book, so full of facts, requires much time to check, the reviewer did not come across any gross deficiencies either in the subject matter or literature references. No doubt it is true that the standard of presentation of the subject matter, especially of the discussion of the fundamentals, has not been uniform in different chapters, but this could not perhaps be helped in a compilation where so many different specialists participated.

The new chapters on "Automatic Control" (which includes most of the essential parts of the chapter on "Temperature Control" of Ed. 2) and "Automatic Recording" have perhaps been included on account of the fact that in near future, the chemists and the chemical engineers will be called upon to know quite a bit about these subjects. The chapter on "Weighing" will be very welcome to the chemists. The author seems to have taken great pains to collect valuable information on the design and testing of balances and on the procedures of weighing. The chapter on "Determination of Particle Size and Molecular Weight" deals with the various methods employed for studying polydisperse systems and the interpretation of the results derived therefrom. Polymer chemists will be particularly interested in this chapter.

Of the chapters retained from Ed. 2, that on "Determination of Viscosity" is practically rewritten and would prove to be more useful than that of the previous edition. The chapter on "Determination of Surface and Interfacial Tension", which replaces that on "Properties of Monolayers and Duplex Films", is largely rewritten and the treatment is restricted to consideration of the properties of monolayers at air-water and oil-water interfaces.

The remaining chapters are practically unchanged although new tables, figures, examples and discussions have been incorporated in some. The reviewer congratulates the editor for having done a fine job again and agrees wholeheartedly with him when he expresses his gratitude to the publishers "not only for their expert handling of technical literature, but for their willingness to undertake a new edition instead of a less onerous, more remunerative, but for the user less satisfactory, reprinting of the second edition".

P.B.

Kinetics of Electrode Processes and Null Points of Metals.—By L. I. Antropov. Council of Scientific & Industrial Research, New Delhi, 1960. Price Rs. 5/- (7s. 6d.).

The Nernst Potential of a metal is referred to the arbitrary zero potential of a normal hydrogen electrode. Prof. Antropov replaces this by what he terms as the ϕ-potential, the reference zero being the null point, *i.e.*, the potential at which the charge of the metal in contact with its ions is zero. According to him the ϕ-potential is more fundamental in so far as the electrochemical properties of metals are concerned.

In order to apply this concept to interpret electrodeposition of metals (Ch. III), corrosion of metals (Ch. V), and electroreduction of organic compounds (Ch. IV) and also to predict these processes, the author classifies the metals into two distinct groups based on the mechanism of hydrogen overvoltage of these metals.

The topics discussed in this small volume have been presented lucidly and convincingly with suitable experimental materials and examples, where necessary.

The examples cited of the success of the concept are fairly extensive but not comprehensive. One of the most important data for the calculation of the ϕ-potential is the null point of a metal. As the author himself admits, the accuracy reported of the values of null points is not high. Moreover, different methods have to be employed for its evaluation in the case of different metals. In view of this it would have been interesting to compare, where possible, the null points of metals by several methods and obtain an idea of the limits of accuracy.

It is very unfortunate that this small volume printed in one of our premier printing concerns is not free from printing lapses. The reviewer could find as many as 30 such mistakes, not all of minor nature. The book has been priced too high.

S.K.M.

Technique of Organic Chemistry. Volume I. Physical Methods of Organic Chemistry. Part II. Third Edition, 1960. Edited by Arnold Weissberger. Pp. 1797 + xxi. Price $21.50.

The third edition under review of Part II of Volume I of the very important series of Weissberger's Technique of Organic Chemistry is not at all a reprint of the second edition but incorporates several improvements giving it an almost new appearance. Some of the topics have been brought up-to-date and some partly rewritten by new authors. Moreover, the topics have been rearranged in four Parts of this Volume with a view to presenting as far as possible the closely allied ones in one Part. Consequently several of the topics, appearing in other Parts of this volume in its earlier publications together with some new topics have appeared in this Part. The selection of the topics has been decidedly advantageous. As a result of these changes the present volume has swollen into about 1800 pages.

The majority of the techniques discussed in this Part have long established applications in various fields of research, not particularly limited to organic chemistry. There are some, however, like X-ray microscopy, microspectroscopy, neutron diffraction, etc., which are new but have justified their inclusion because of their great promise as complementary tools for the chemist.

Throughout the pages of this Part one is constantly reminded of a very valuable work done with care and precision. The articles are authoritative and critical, and the theoretical principles underlying each are presented with the lucidity, which treatises of this type deserve. As far as the reviewer can judge, some of the mathematical analyses may be beyond the scope of conventional organic chemists without further assistance, but they will not deter them for making a good use of the techniques themselves. The details of the experimental procedures, description of apparatuses, indications of the order of precision attained by each, etc. hardly leave anything that is relevant and important.

Although primarily meant for the use of organic chemists the articles will be almost equally useful to other workers interested in the application of physical measurements to their problems.

The references are up-to-date. The excellence of printing, reproduction of diagrams and general get-up has been maintained. The printing lapses are but rare.

S.K.M.

Molecular Structure. The Physical Approach.—By J. C. D. Brand and J. C. Speakman. Published by Edward Arnold (Publishers) Ltd. Pages 300 + viii. Price 30s.

The title gives an impression of a very wide scope of the book. It discusses, however, only some aspects—two methods, the spectroscopy and diffraction. The authors take the 'word structure of molecule to connote more than just the relative position of its atoms', yet they have not included 'all ideas that might be associated with the notion of atoms-united-to-form-a-molecule' to keep the size of the book limited.

The authors start with a short historical and general introduction. Next they deal with symmetry, which is well justified in view of the importance of the subject in the understanding of molecular structure. Then follows a chapter on elementary wave mechanics. Of the rest, four chapters are devoted to rotation spectra, nuclear magnetic resonance, vibration spectra and polarisability and Raman effect and two chapters on X'-ray analysis and electron diffraction methods. The principles have been discussed with only a few examples. The last chapter is a short appraisement of the methods.

The book is written for the Honours students in Physical Chemistry and research workers in the other branches of Chemistry. The authors concentrate more on principle than on practice The inclusion of more examples and a more detailed concluding chapter would make the book more interesting.

The book is moderately priced. The students of Physical Chemistry, in particular, will find the book useful.

S.A.

Atoms, Molecules and Chemical Change.—By E. Granwald and R. H. Johnson. Published by Prentice Hall Inc., 1960. Pages 252 + xii. Price $ 6.00.

This is the age of science and a cursory knowledge of science is sought to be imparted even to non-science students by every University of the world. In the field of chemistry as well as in other branches of science, though the knowledge has extended beyond the world of perception to the atomic and even subatomic, application of this knowledge now abounds in a large measure in the form of electronic instruments, nuclear reactors, isotopic tracers, and so forth. The modern educated man, who will have occasion to use them, should naturally evince a desire to understand the broad principles underlying them.

This volume is an attempt in that respect. It presents the basic facts of chemistry leading to nuclear reactions in course of one semester course to non-science students.

The book takes up only a few stoichiometric calculations as examples and omits oxidation-reduction, chemical kinetics, colligative properties of solutions, and descriptions of single elements and their compounds generally and does so to keep down its volume. The theme of structure of matter, however, is very methodically developed through historical and logical sequence in an admirable way. There are 17 chapters, the first four being devoted to bring out the distinction of mixture and compound and the laws of chemical compounding. Chapters 5-7 introduce the concept of the molecular theory of matter, its energy relations in different states of aggregation and interrelation of kinetic and potential energy with the internal energies of the system. Chapters 8-11 describe the evolution of the concept of modern electronic structure of atoms and re-reading of the Periodic Table in this new light. Principles of compound formation are developed in two chapters, 12 and 13, and architecture and reactions of covalent compounds in Chapters 14 & 15. The last two Chapters 16 & 17 are devoted to the study of nucleus and nuclear reactions. A glossary of scientific terms, leading questions for each chapter and a detailed index evince the care and attention, the authors have taken in writing the book.

The book gives promise of a wide appreciation and is worth the attention of learned makers of syllabi of the universities as a practical example of a bold curriculum, for non-science students interested in Nuclear Chemistry.

K.L.M.

Chemical Analysis of Resin-Based Coating Materials.—Edited by C. P. A. Kappelmeier. Published by Interscience Publishers, New York and London. Pages 630. Price $19.50.

Published soon after the demise of Dr. Kappelmeier, the book is like a crown to his life-long devotion to the analytical problems related to the chemistry of coating composition. The book is an attempt to cover comprehensively the various methods of analysis for identification and determination of various constituents of coating materials : Paints, Varnishes, Lacquers and related materials. There are three sections in the book. Analysis of Oil-based Coating Materials, Analysis of Lacquers and selected chapters on the Analysis of Coating Materials—last one being mainly concerned with the methods of identification and some modern analytical tools. Each section is subdivided into several chapters—all of them written by specialists in their own fields—and many by Dr. Kappelmeier himself. There is an experimental section along with most of the chapters which give testing procedures in some detail. References to published papers have been made at the end of each chapter.

The main criticism against the book is that devotion of space to different chapters is not entirely according to the importance of the subject concerned. While chemistry of Rosin and Alkyd Resins have been covered in detail, comparatively little space has been devoted to the recent developments in the synthetic field. Information on the techniques of ultraviolet and infrared spectroscopy is inclined to be somewhat scrappy. Little attempt has been made to explain the chemistry involved in different tests for identification and estimation of compounds. In spite of these drawbacks the book contains a vast amount of valuable information, which is seldom to be found in a single volume. Absence of such a book on the analytical problems of coating materials was keenly felt by everybody connected with the field and its guidance will be most welcome by them.

S.B.

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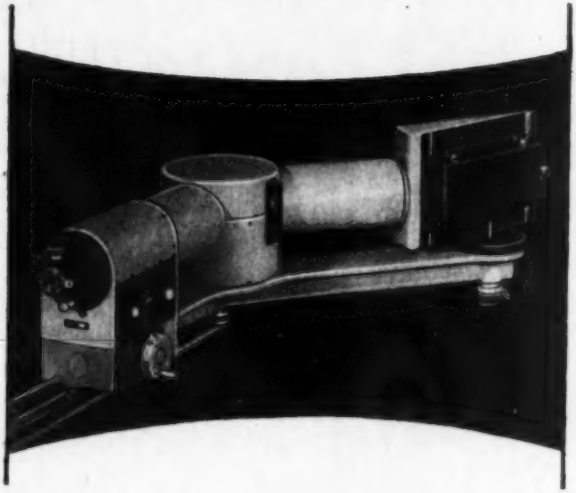

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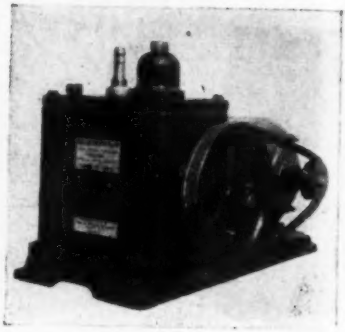

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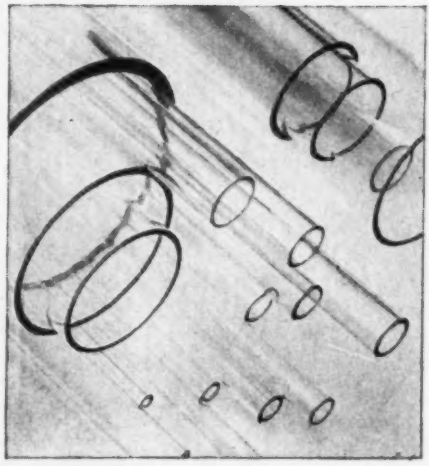

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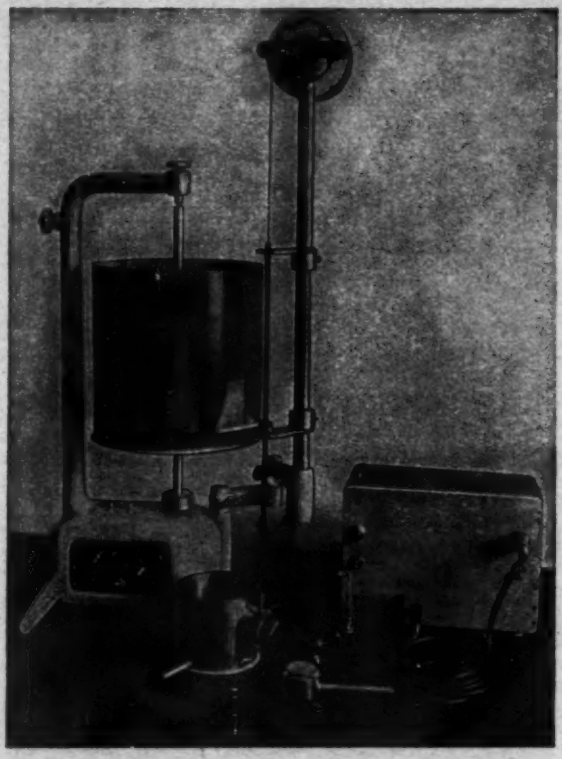

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